Predictors of Survival Time Among HIV-Infected Adults After Initiating Anti-Retroviral Therapy in Kombolcha Town: A 5-Year Retrospective Cohort Study

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Background: Antiretroviral therapy (ART) enhances the survival of HIV-infected patients by reducing viral load and increasing CD4. As CD4 count increases, patients are more protected against opportunistic infections. In developing countries including Ethiopia, there were limited studies about the survival benefit of ART particularly no study in Kombolcha Town. Thus, this study was aimed to address the gap.

Methods: A hospital-based retrospective cohort study was employed in Kombolcha town among 510 patients’ records from January 2015 to December 2019. A systematic random sampling technique was used to select patient records. The collected data were checked, coded, and entered into Epidata version 4.6 and exported to Statistical Package for Social Sciences version 26 for data cleaning and analysis. Kaplan–Meier was used to estimate the probability of category of each predictor and a log rank test was used to compare survival curves. Bivariate and multivariate Cox-regression were employed using a 95% CI and variables with p-value <0.05 were declared as predictors of poor survival time.

Results: In this cohort, out of 510 HIV-infected patients, 39 (7.65%) were died, and 471 (92.35%) were censored. Fair drug adherence (AHR=6.88, 95% CI: 4.31–24.04), Poor drug adherence (AHR=9.58, 95% CI: 8.72–30.97), CD4 count <50 cell/µL (AHR=9.38, 95% CI: 1.48–59.31), CD4 count 50–99 cell/µL (AHR=9.67, 95% CI: 1.80–51.73), bedridden (AHR=9.5, 95% CI: 4.49–18.66), opportunistic infections (AHR=4.58, 95% CI: 1.20–15.65), weight <60kg (AHR=2.48, 95% CI:1.59, 10.38), WHO stage III (AHR=3.56, 95% CI: 1.71–17.89), WHO stage IV (AHR=4.42, 95% CI:1.75–25.93) were predictors of poor survival time.

Conclusion: The Kaplan–Meier result showed that the estimated median survival time of patients after ART initiation in Kombolcha town was higher (32 months) as compared to other studies. Poor drug adherence, WHO stage III & IV, Lower baseline CD4 count, presence of opportunistic infections, weight <60kg, and being bedridden were predictors of poor survival time. Thus, early initiation of ART ought to be encouraged among HIV-infected patients and good patient counseling on the level of adherence should be strengthened.

Keywords: survival time, predictors, Kombolcha, HIV/AIDS

Introduction

Antiretroviral therapy (ART) is defined as the use of a combination of three or more antiretroviral drugs for the treatment of HIV infection, and it involves lifelong treatment.¹ WHO (2015) recommended that all HIV-positive patients start ART irrespective of clinical staging and CD4 count.

United Nations program on HIV/AIDS (USAID) and partners proposed three new and ambitious targets, three 90’s. These targets are diagnosing 90% of people living with HIV, providing ART to 90% of for those diagnosed with HIV, and achieving viral suppression for 90% of patients receiving treatment.² To improve HIV care and treatment to achieve the
goal of 90–90–90 following strategies are crucial. Working with religious leaders; implementing new programs (self-HIV testing, house-to-house HIV testing, community ART distribution, and teach-test-treat –link strategy); decentralizing ART services in health posts and private clinics; integrating HIV care services with mental illness and other non-communicable diseases; filling gaps in legislation issues related with HIV status disclosure and traditional helping practices.3

Globally, around 36,990 new HIV infections have occurred.4 In Ethiopia, 67% of people living with HIV know their status, 88% of them are on treatment, and 86% of people are on treatment have viral suppression. By 2020, 79% of people living with HIV know their status, of which 96–99% are on ART and 86% of viral suppression.5

ART enhances the survival of HIV-positive patients by reducing viral load and increasing CD4. As CD4 count increases, patients are more protected against opportunistic infections. In developing countries including Ethiopia, there were limited studies about the survival benefit of ART particularly no study in Kombolcha Town. Thus, this study was aimed to address the gap.

Materials and Methods
Study Design and Study Area Description
Five (5) years retrospective cohort study was conducted from 1 January 2015 to 30 December 2019 in Kombolcha town health centers. Kombolcha town is located in North Eastern part of Ethiopia at a distance of 379 kilometer from the capital city, Addis Ababa. The town had a total population of 162,533 (77,041 were males and 85,492 were females (CSA, 2013)). In Kombolcha town there were 4 public health centers, 12 health posts and 16 private clinics. Three public health centers were provided ART services for 3348 HIV-infected patients.

Study Participants and Eligibility Criteria
All HIV-infected patients who were enrolled in ART clinic from January 2015 to December 2019 in Kombolcha town health centers were study participants. All HIV-infected patients aged greater than 18 years and who started ART in three health centers were included in the study whereas age <18 years, patients who started ART outside the study health centers and had incomplete medical records were excluded from the study.

Sample Size Determination and Sampling Technique
The sample size was calculated using double population proportion formula by using Epi info version 7.1 through considering different factors. Adherence was chosen as the main exposure because it gave the maximum sample size. Statistical assumptions were considered (ie power = 80%, confidence interval = 95%, Ratio (number in exposed: unexposed) =1:1, estimated proportion of mortality in Ethiopia taken as 9.9% for non-exposed group). Hence, 512 patients living with HIV/AIDS and started ART were included in this study. Study participants were selected from the registration book by using systematic random sampling technique. The sample interval was calculated as 3348 divided by 512. The sample was allocated proportionally to three health centers (Kombolcha 03, Kombolcha 02, and Kombolcha 05). Profiles of all patients on ART between 1 January 2015, and 30 December 2019 was evaluated from available standard national medical registers, which have been adopted by the Ethiopian Ministry of Health.

Data Collection and Quality Management
The pre-prepared data retrieval (data abstraction tool) form was developed from records of the Federal Ministry of Health of Ethiopia, ART entry and follow-up forms, patient records, laboratory requests and computer data. The information related to socio-demographic, medical, and behavioral related factors was retrieved from ART case notes using pretested information extraction tool during the data collection period. To ensure data quality, data was collected by ART staff nurses and the tool was pretested in 5% at Dessie health center. The training was given to data collectors and supervisors regarding the data abstraction technique. Data quality was also controlled through continuous supervision and ongoing formative checkup for completeness and consistency of responses.
Outcome Variable
The outcome variable is the time from initiation of ART to an event, categorized to death and censored (alive, transferred out, and lost-to-follow-up).

Independent Variables
Socio-demographic characteristics (Age, Sex, Marital status, Educational status, Occupation).

Base Line Factors (Weight, Height, WHO clinical staging, CD4 count, Hemoglobin level, functional status, past medication).

ART treatment (ART eligibility criteria, OI prophylaxis, Regimens given at follow up time, drug regimen change).

Patient Follow Up Factors (Date of HIV confirmed, Eligible date, duration ART, Drug side effect, TB screened and prophylaxis, TB treatment and co-trimoxazole preventive therapy, Recent ARV adherence, Recent CD4 count, Recent Hemoglobin).

Operational Definitions
Drop out: if a patient discontinued ART for at least three months as recorded by the ART physician.6

Lost: if a patient discontinued ART for 1 to 3 months as recorded by the ART physician.6

Good Adherence: if the percentage of missed dose is >95% (<2 doses of 30 doses or <3 doses of 60 doses) as documented by ART physicians.6

Fair Adherence: if the percentage of missed dose is 85–95% (3–5 doses of 30 doses or 3–9 doses of 60 doses) as documented by ART physicians.6

Poor Adherence: if the percentage of missed dose <85% (>6 doses of 30 doses or >9 doses of 60 doses) as documented by physicians.6

Survival time: The number of months from initiation of ART until the death of the patient.7

Event case: all HIV patients who will die after ART medication was initiated.

Censored: A patient does not develop event (transferred out, lost to follow up and alive).

Baseline: is the measurement taken nearest to the date of ART initiation.

Prophylaxis: aims to avoid either the first occurrence of infections (primary prophylaxis) or their recurrence (secondary prophylaxis or maintenance).1

Data Management and Analysis
The collected data was entered into EpiData version 4.6 and exported to SPSS version 26.0 for data cleaning and analysis. The patients’ cohort characteristics were described in terms of the mean value for continuous data and percentage for categorical data. Death was confirmed by reviewing the death registration in the hospital, or registration by ART adherence supporter through calling using the registered phone number and individuals alive. Finally, the outcome of each subject was dichotomized into censored or death. Kaplan–Meier was used to estimate the probability of category of each predictor and a Log rank test was used to compare survival curves. Bivariate (crude hazard ratio) and multivariate (adjusted hazard ratio) Cox-regression were employed using a 95% confidence interval (CI). From bivariable Cox-regression, variables with p-value<0.25 were candidate for Cox-regression. Then, from Cox-regression variables with p-value <0.05 were declared as predictors of poor survival time.

Results
Socio-Demographic Characteristics
The majority, 289 (56.7%) of study participants were females and the mean (±SD) age of respondents was 39.9 (±12.168) years. Over half, 262 (51.4%) of participants were married and 359 (70.4%) of them had lived in urban (Table 1).
Baseline Clinical Characteristics
The majority, 214 (42%) of participants had CD4 count ≥350 and 194 (38%) of them had classified under WHO stage 1. Most, 409 (80.2%) of them had hemoglobin level ≥10g/dl with working 421 (82.5%) functional status at the baseline. Additionally, 213 (41.8%) had opportunistic infections (Table 2).

Treatment and Patient Follow Up Characteristics
Three-fourths, 387 (75.9%) of participants had taken CPT (Co-trimoxazole preventive therapy) and 386 (75.7%) of them had taken the drug regimen AZT-3TC-EFV. Most, 424 (83.1%) and one-fourths, 130 (25.5%) of participants respectively had good drug adherence and drug side effect (Table 3).

Pattern of Death
As life table showed, the pattern of death with time intervals among HIV-infected adults on ART revealed that the proportion of surviving decreases as the duration of ART increases (Table 4).

Survival Status HIV-Infected Patients After Initiation of ART
The study participants were followed for 60 months and the follow-up outcome was categorized into died and censored (patients who transfer out, lost to follow-up, and survived beyond the study period). In this cohort, out of 510 HIV-infected...
### Table 2 Baseline Clinical Characteristics of HIV-Infected Adults After Initiating ART in Kombolcha Town from January 2015 to December 2019 (n=510)

| Variable               | Categories | Censored | Death | Total |
|------------------------|------------|----------|-------|-------|
| **CD4 count**          |            |          |       |       |
| <50                    | 16(3.4%)   | 4(10.3%) | 20(3.9%) |
| 50–99                  | 16(3.4%)   | 10(25.6%) | 26(5.1%) |
| 100–199                | 111(23.6%) | 9(23.1%) | 120(23.5%) |
| 200–349                | 120(25.5%) | 10(25.6%) | 130(25.5%) |
| ≥350                   | 208(44.2%) | 6(15.4%) | 214(42.0%) |
| **WHO clinical staging** |            |          |       |       |
| Stage I                | 188(39.9%) | 6(15.4%) | 194(38.0%) |
| Stage II               | 176(37.4%) | 10(25.6%) | 186(36.5%) |
| Stage III              | 70(14.9%)  | 11(28.2%) | 81(15.9%) |
| Stage IV               | 37(7.7%)   | 12(30.8%) | 49(9.6%) |
| **Functional status**  |            |          |       |       |
| Working                | 404(85.8%) | 17(43.6%) | 421(82.5%) |
| Ambulatory             | 60(12.7%)  | 15(38.5%) | 75(14.7%) |
| Bedridden              | 7(1.5%)    | 7(17.9%) | 14(2.7%) |
| **Hemoglobin level (g/dl)** |        |          |       |       |
| <10                    | 87(18.5%)  | 14(35.9%) | 101(19.8%) |
| ≥10                    | 384(81.5%) | 25(64.1%) | 409(80.2%) |
| **Opportunistic Infections** |        |          |       |       |
| Yes                    | 203(43.1%) | 10(25.6%) | 213(41.8%) |
| No                     | 268(56.9%) | 29(74.4%) | 297(58.2%) |

### Table 3 Treatment and Patient Follow Up Characteristics of HIV-Infected Adults After Initiating ART in Kombolcha Town from January 2015 to December 2019 (n=510)

| Variable                  | Categories               | Censored | Death | Total |
|---------------------------|--------------------------|----------|-------|-------|
| **ART eligible criteria** | CD4 <200                 | 108(22.9%) | 14(35.9%) | 122(23.9%) |
| WHO stage IV              | 55(11.7%)                | 12(30.8%) | 67(13.1%) |
| WHO stage II & TLC        | 175(37.2%)               | 8(20.5%) | 183(35.9%) |
| Test and treat            | 133(28.2%)               | 5(12.8%) | 138(27.1%) |
| **OIs prophylaxis given** | Not given                | 14(3.0%)  | 0(0.0%) | 14(2.7%) |
| CPT                       | 359(76.2%)               | 28(71.8%) | 387(75.9%) |
| INH                       | 95(20.2%)                | 11(28.2%) | 106(20.8%) |
| Others                    | 3(0.6%)                  | 0(0.0%)  | 3(0.6%) |
| **Regimen given**         | 1a(30)=d4t(30)-3TC-NVP   | 8(1.7%)  | 2(5.1%) | 10(2.0%) |
| 1a(40)=d4t(40)-3TC-NVP    | 1(0.2%)                  | 0(0.0%)  | 1(0.2%) |
| 1b(40)=d4t(30)-3TC-EFV    | 17(3.6%)                 | 0(0.0%)  | 17(3.3%) |
| 1b(40)=d4t(40)-3TC-EFV    | 19(4.0%)                 | 5(12.8%) | 24(4.7%) |
| 1c= AZT-3TC-NVP           | 9(1.9%)                  | 0(0.0%)  | 9(1.8%) |
| 1d= AZT-3TC-EFV           | 354(75.2%)               | 32(82.1%) | 386(75.7%) |
| 1E=TDF-3TC-EFV            | 8(1.7%)                  | 0(0.0%)  | 8(1.6%) |
| 1F=TDF-3TC-NVP            | 55(11.7%)                | 0(0.0%)  | 55(10.8%) |
| **TB prophylaxis**        | No                       | 44(9.3%) | 8(20.5%) | 52(10.2%) |
| Yes                       | 427(90.7%)               | 31(79.5%) | 458(90.8%) |
| **ART adherence**         | Good                     | 420(89.2%) | 12(30.8%) | 424(83.1%) |
| Fair                      | 45 (9.6%)                | 12(30.8%) | 57(11.2%) |
| Poor                      | 6(1.3%)                  | 23(59.0%) | 29(5.7%) |
| **ART side effect**       | Yes                      | 99(21.0%) | 31(79.5%) | 130(25.5%) |
| No                        | 372(79.0%)               | 8(20.5%) | 380(74.5%) |
patients on ART, 471 (92.35%) were censored and 39 (7.65%) have died. From 471 censored patients, 430 (84.31%) were alive, 26 (5.1%) transferred out and 15 (2.94%) lost to follow up (Figure 1). The median survival time was 32 months. The cumulative probability of survival at 20, 40, and 60 months after ART initiation was 93%, 87%, and 83%, respectively (Figure 2). Starting co-trimoxazole therapy (CPT) early increases the survival function of HIV infected patients (Figure 3). Having good adherence enhances the survival rate of HIV-infected patients (Figure 4). Early initiation of ART is crucial to enhance the survival rate of HIV-infected patients. Patients who started ART in WHO stage I had better survival outcomes as compared to WHO stage IV (Figure 5).

Table 4 Life Table Revealing Pattern of Death with Time Intervals of HIV-Infected Adults After Initiating ART in Kombolcha Town from January 2015 to December 2019

| Interval Start Time | Number Entering Interval | Number Withdrawing During Interval | Number Exposed to Risk | Number of Terminal Events | Proportion Terminating | Proportion Surviving | Cumulative Proportion Surviving at End of Interval |
|---------------------|--------------------------|-----------------------------------|------------------------|---------------------------|-----------------------|---------------------|--------------------------------------------------|
| 0                   | 510                      | 70                                | 475.000                | 0                         | 0.00                  | 1.00                | 1.00                                             |
| 10                  | 440                      | 81                                | 399.500                | 10                        | 0.03                  | 0.97                | 0.97                                             |
| 20                  | 349                      | 66                                | 316.000                | 13                        | 0.04                  | 0.96                | 0.93                                             |
| 30                  | 270                      | 70                                | 235.000                | 8                         | 0.03                  | 0.97                | 0.90                                             |
| 40                  | 192                      | 97                                | 143.500                | 6                         | 0.04                  | 0.96                | 0.87                                             |
| 50                  | 89                       | 84                                | 47.000                 | 2                         | 0.04                  | 0.96                | 0.83                                             |
| 60                  | 3                        | 3                                 | 1.500                  | 0                         | 0.00                  | 1.00                | 0.83                                             |

Figure 1 Survival status (outcome of follow-up) of HIV-infected adults after initiating ART in Kombolcha town from January 2015 to December 2019.
Figure 2 The probability of survival time of HIV-infected adults after initiating ART in Kombolcha town from January 2015 to December 2019.

Figure 3 Survival functions of HIV-infected adults after initiating ART in Kombolcha town by baseline CPT from January 2015 to December 2019.
Kaplan–Meier Analysis on Socio-Demographic Characteristics
Kaplan–Meier’s analysis revealed that participants categorized in age 18–29 years had better survival than age ≥60 years (56.96 months, 95% CI: 54.8–59.12 Vs 49.22 months, 95% CI: 44.29–54.14). Participants who had lived in rural areas showed less survival time than urban residents (53.41 months, 95% CI: 50.85–55.96 Vs 56.48, 95% CI: 55.14–57.82). Likewise, participants who had not attended any education were less survival time than those who had attended primary education (53.5 months, 95% CI: 51.22–55.77 Vs 57.15 months, 95% CI: 55.54–58.77) (Table 5).

Kaplan–Meier Analysis on Baseline Characteristics
Patients having weight ≥60 kg had better survival time than <60 kg (58.02 months, 95% CI: 56.13–59.88 Vs 55.3 months, 95% CI: 53.84–56.75). Patients who had CD4 Count ≥350 were better surviving as compared to having CD4 count <50 (58.46 months, 95% CI: 57.26–59.67 Vs 40.08 months, 95% CI: 33.0–47.15). Patients who had good medication adherence were lived better than those who had poor adherence (59.45 months, 95% CI: 58.92–60.0 Vs 32.47 months, 95% CI: 27.6–37.34). Patients who had opportunistic infections were less survive than their counterparts (54.96 months, 95% CI: 53.25–56.67 Vs 57.31, 95% CI: 55.73–58.9) (Table 6).

Predictors of Mortality After Initiation of ART
From multivariable Cox regression model, fair and poor drug adherence, CD4 count<50andCD4 count 50–99, functional status of Bedridden, presence of OIs, Weight < 60kg, WHO staging III, and WHO staging IV were independent predictors of mortality. The hazard of patients’ mortality was 6.88 times higher among adults with fair drug adherence than patients who had good adherence to ART (AHR= 6.88, 95% CI: 4.31–24.04). Likewise, the hazard of adult mortality was 9.58 times higher among adults with poor drug adherence than adults who had good adherence to ART (AHR=9.58, 95% CI: 8.72–30.97). The hazard of mortality was 9.67 times higher among adults with CD4 count < 50.
than adults who had CD4 count ≥350 (AHR = 9.67, 95% CI: 1.48–59.31). Similarly, the hazard of mortality was 9.38 times higher among adults with CD4 count 50–99 than adults who had CD4 count ≥350 (AHR = 9.67, 95% CI: 1.80–51.73). The hazard of mortality was 9.5 times higher among bedridden patients than patients who had working functional status (AHR=9.5, 95% CI: 4.49–18.66). The risk of mortality was 4.58 times higher among patients having opportunistic infections than their counterparts (AHR=4.58, 95% CI: 1.20–5.65). The hazard of mortality was 2.48 times higher among patients with body weight <60kg than their counterparts (AHR= 2.48, 95% CI: 1.59–10.38). The hazard of mortality was 3.56 times higher among patients with WHO clinical stage III than patients having WHO clinical stage I (AHR=3.56, 95% CI: 1.71–17.89). Likewise, the hazard of mortality was 4.42 times higher among patients with WHO clinical stage IV than patients having WHO clinical stage I (AHR=4.42, 95% CI: 1.75–25.93) (Table 7).

Discussion
This cohort study was identified predictors of survival time among HIV-infected adults after initiation of ART. Accordingly, fair and poor ART adherence, CD4 count<50andCD4 count 50–99, functional status of bedridden, presence of OIs, Weight < 60kg, and WHO clinical staging III and IV were independent predictors of poor survival time.

In this cohort, 7.65% (95% CI: 5.21–10.42) patients have died. This is in line with other studies in Aksum hospital (8.85%)8 Oromia region (10.3%),9 Eastern Ethiopia (5.9%),10 Tigray central zone (7.5%),11 Jinka hospital (10%),12 Gofa zone hospital (7.5%)13 and Latin America (7.3%).14 However, this finding is lower than studies in Hiwot Fana teaching hospital (11.9%),15 Kambata tambaro zone (12.63%),16 Malawi (12.6%),17 Durban, South Africa (16%)18 and India (13%, 16.1%).19,20 The difference might be due to differences in socioeconomic characteristics and duration of follow-up.

The mortality hazard ratio of those with baseline weight <60kg compared with those with baseline weight ≥60kg is 2.48 (95% CI: 1.59–10.38). This is supported by other studies, Gambia,21 Aksum8 (AHR = 2.3, 95% CI:1.24, 4.55),
The hazard of patients’ mortality was 6.88 times higher among adults with fair drug adherence than patients who had good drug adherence (AHR = 6.88, 95% CI: 4.31–24.04). Likewise, the hazard of adult mortality was 9.58 times higher among adults with poor drug adherence than adults who had good adherence to ART (AHR = 9.58, 95% CI: 8.72–30.97). This is consistent with other studies in Nekemet, Kambata Tambaro Zone (AHR = 3.8, 95% CI: 1.88, 7.96) Goffa zone, Canada. The hazard of mortality was 9.67 times higher among adults with CD4 count <50 than adults who had CD4 count ≥350 (AHR = 9.67, 95% CI: 1.48–59.31). Similarly, the hazard of mortality was 9.38 times higher among adults with CD4 count 50–99 than adults who had CD4 count ≥350 (AHR = 9.67, 95% CI: 1.80–51.73). This is congruent with other studies; India, Cameron, Durban, South Africa, Canada, Latin America, Singapore, Ethiopia.

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The hazard of mortality was 9.5 times higher among bedridden patients than patients who had working functional status (AHR = 9.5, 95% CI: 4.49–18.66). This finding is supported by similar studies in India, eastern Ethiopia, Tigray central zone, Jinka Hospital, kamata tambaro zone, Goffa zone public hospitals. The risk of mortality was 4.58 times higher among patients having opportunistic infections than their counter parts (AHR = 4.58, 95% CI: 1.20–5.65). This is supported by South Africa, kambata tambaro zone, Goffa zone public hospitals.

The hazard of mortality was 3.56 times higher among patients with WHO clinical stage III than patients having WHO clinical stage I (AHR=3.56, 95% CI: 1.71–17.89). Likewise, the hazard of mortality was 4.42 times higher among patients with WHO clinical stage IV than patients having WHO clinical stage I (AHR=4.42, 95% CI: 1.75–25.93). This is supported by studies in Latin America, Oromia region, eastern Ethiopia, Cameron, India, Jinka hospital, Zewuditu hospital, teaching hospitals in Ethiopia, Hiwot Fana hospital, and Malawi.

Table 5 Kaplan–Meier Analysis on Socio-Demographic Characteristics of HIV-Infected Adults After Initiating ART in Kombolcha Town from January 2015 to December 2019

| Variables                  | Estimated Survival Month | Standard Error | 95% Confidence Interval |
|---------------------------|--------------------------|----------------|-------------------------|
| Sex                       |                          |                |                         |
| Male                      | 55.96                    | 0.92           | 54.16–57.77             |
| Female                    | 55.88                    | 0.82           | 54.26–57.50             |
| Marital status            |                          |                |                         |
| Single                    | 54.02                    | 1.92           | 50.24–57.80             |
| Married                   | 56.72                    | 0.76           | 55.22–58.21             |
| Divorced                  | 55.71                    | 1.26           | 53.22–58.20             |
| Widowed                   | 53.47                    | 1.60           | 50.33–56.61             |
| Separated                 | 45.00                    | 0.00           | 45.00–45.00             |
| Place of residence        |                          |                |                         |
| Rural                     | 53.41                    | 1.30           | 50.85–55.96             |
| Urban                     | 56.48                    | 0.68           | 55.14–57.82             |
| Occupational status       |                          |                |                         |
| Farmer                    | 52.95                    | 1.45           | 50.10–55.81             |
| Merchant                  | 55.70                    | 1.52           | 52.71–58.70             |
| Governmental              | 55.42                    | 2.38           | 50.76–60.09             |
| Non- governmental         | 56.75                    | 0.75           | 55.27–58.22             |
| Educational status        |                          |                |                         |
| Primary                   | 57.15                    | 0.82           | 55.54–58.77             |
| Secondary                 | 55.26                    | 1.33           | 52.65–57.88             |
| Tertiary                  | 54.60                    | 2.23           | 50.22–58.97             |
| Not educated              | 53.50                    | 1.16           | 51.22–55.77             |
| Age in years              |                          |                |                         |
| 18–29                     | 56.96                    | 1.10           | 54.80–59.12             |
| 30–44                     | 56.50                    | 0.83           | 54.87–58.12             |
| 45–59                     | 54.58                    | 1.47           | 51.69–57.46             |
| ≥60                       | 49.22                    | 2.51           | 44.29–54.14             |


Conclusion
The Kaplan–Meier result showed that the estimated median survival time of patients after ART initiation in Kombolcha town was higher (32 months) as compared to other studies. Poor drug adherence, WHO stage III & IV, Lower baseline CD4 count, presence of opportunistic infections, weight < 60kg, and being bedridden were predictors of poor survival time. Thus, early initiation of ART ought to be encouraged among HIV-infected patients and good patient counseling on the level of adherence should be strengthened.

Abbreviations
AIDS, acquired immune deficiency syndrome; AHR, adjusted hazard ratio; ART, antiretroviral therapy; CHR, crude hazard ratio; CI, confidence interval; HIV, human immunodeficiency virus; MOH, Ministry Of Health.

Table 6 Kaplan–Meier Analysis on Baseline Characteristics of HIV-Infected Adults After Initiating ART in Kombolcha Town from January 2015 to December 2019

| Variable                                | Estimated Survival Time (Month) | Standard Error | 95% CI        |
|-----------------------------------------|---------------------------------|----------------|---------------|
| Weight in Kg                            |                                 |                |               |
| < 60                                    | 55.30                           | 0.74           | 53.84–56.75   |
| ≥60                                     | 58.02                           | 0.95           | 56.13–59.88   |
| CD4 Count                               |                                 |                |               |
| < 50                                    | 40.08                           | 3.61           | 33.00–47.15   |
| 50–99                                   | 50.74                           | 3.71           | 43.45–58.03   |
| 100–200                                 | 55.21                           | 1.19           | 52.87–57.55   |
| 200–350                                 | 54.67                           | 1.25           | 52.22–57.13   |
| ≥350                                    | 58.46                           | 0.61           | 57.26–59.67   |
| WHO clinical staging of HIV             |                                 |                |               |
| Stage I                                 | 58.24                           | 0.69           | 56.82–59.60   |
| Stage II                                | 57.24                           | 0.83           | 55.60–58.88   |
| Stage III                               | 53.59                           | 1.77           | 50.11–57.06   |
| Stage IV                                | 44.06                           | 3.09           | 37.99–50.12   |
| Functional status                       |                                 |                |               |
| Working                                 | 57.82                           | 0.51           | 56.81–58.82   |
| Ambulatory                              | 48.81                           | 2.2            | 44.49–53.12   |
| Bedridden                               | 32.59                           | 4.26           | 24.23–40.96   |
| Hemoglobin level (g/dl)                 |                                 |                |               |
| < 10                                    | 50.72                           | 1.71           | 47.35–54.09   |
| ≥10                                     | 56.76                           | 0.61           | 55.54–57.97   |
| Eligible criteria                       |                                 |                |               |
| CD4 < 200                               | 53.47                           | 1.36           | 50.80–56.15   |
| WHO stage IV                            | 49.77                           | 2.27           | 45.31–54.22   |
| WHO stage II & TLC                      | 57.68                           | 0.78           | 56.14–59.22   |
| Test and treat                          | 57.84                           | 0.93           | 56.01–59.67   |
| TB Prophylaxis                          |                                 |                |               |
| No                                      | 50.90                           | 2.74           | 45.51–56.28   |
| Yes                                     | 56.42                           | 0.61           | 55.22–57.61   |
| ARV Adherence                           |                                 |                |               |
| Good                                    | 59.45                           | 0.27           | 58.92–60.0    |
| Fair                                    | 48.80                           | 2.64           | 43.61–53.99   |
| Poor                                    | 32.47                           | 2.48           | 27.60–37.34   |
| Drug side effect                        |                                 |                |               |
| Yes                                     | 48.46                           | 1.70           | 45.13–51.80   |
| No                                      | 58.81                           | 0.41           | 58.01–59.62   |
| OIs                                      |                                 |                |               |
| No                                      | 57.31                           | 0.80           | 55.73–58.90   |
| Yes                                     | 54.96                           | 0.87           | 53.25–56.67   |
| CPT                                      |                                 |                |               |
| Not Given                               | 50.29                           | 1.65           | 47.04–53.53   |
| Given                                   | 57.05                           | 0.50           | 56.05–58.04   |
Table 7 Predictors of Survival Time in Cox-Regression Among HIV-Infected Adults After Initiating ART in Kombolcha Town from January 2015 to December 2019 (n=510)

| Variables                  | Categories | Death | Censored | CHR (95% CI) | AHR (95% CI) |
|----------------------------|------------|-------|----------|--------------|--------------|
| ART adherence              | Good       | 4     | 420      | 3.30(2.72–15.06) | 6.88(4.31–24.04)* |
|                            | Fair       | 12    | 45       | 8.08(6.51–18.31) | 9.58(7.82–30.97)* |
|                            | Poor       | 23    | 6        | 1           | 1            |
| Age in years               | 18–29      | 7     | 127      | 0.27(0.12–0.96)   | 0.37(0.19–2.36)   |
|                            | 30–44      | 16    | 219      | 0.19(0.10–1.02)   | 0.56(0.17–1.62)   |
|                            | 45–59      | 8     | 79       | 0.42(0.35–1.51)   | 0.64(0.21–2.08)   |
|                            | ≥60        | 8     | 46       | 1           | 1            |
| CD4 Count                  | <50        | 4     | 16       | 6.34(1.34–52.32) | 9.67(1.48–59.31)* |
|                            | 50–99      | 10    | 16       | 7.01(1.75–45.21) | 9.38(1.80–51.73)* |
|                            | 100–200    | 9     | 111      | 2.68(1.65–3.76)  | 0.92(0.18–4.72)   |
|                            | 200–349    | 10    | 120      | 3.05(2.12–4.53)  | 0.87(0.19–3.93)   |
|                            | ≥350       | 6     | 208      | 1           | 1            |
| CPT                        | Given      | 25    | 102      | 1           | 1            |
|                            | Not given  | 14    | 369      | 5.35(2.46–7.43) | 3.68(0.37–4.86)   |
| ART side effect            | Yes        | 31    | 99       | 1.86(1.14–3.75) | 1.11(0.28–4.40)   |
|                            | No         | 8     | 372      | 1           | 1            |
| Educational status         | Primary    | 12    | 197      | 1           | 1            |
|                            | Secondary  | 7     | 100      | 1.37(0.82–1.65) | 0.61(0.24–1.55)   |
|                            | Tertiary   | 0     | 29       | 1.36(0.76–1.82) | 1.22(0.31–4.70)   |
|                            | Not educated | 20   | 145      | 2.10(1.32–5.58) | 0.88(0.11–6.82)   |
| Functional Status          | Working    | 17    | 404      | 1           | 1            |
|                            | Ambulatory | 15    | 60       | 5.64(1.35–7.35) | 2.48(0.74–8.30)   |
|                            | Bedridden  | 7     | 7        | 9.64(6.52–14.23)| 9.50(4.49–18.66)* |
| Hemoglobin (g/dl)          | <10        | 14    | 87       | 5.64(2.34–8.47) | 1.11(0.42–2.94)   |
|                            | ≥10        | 25    | 384      | 1           | 1            |
| Occupational status        | Farmer     | 14    | 102      | 1           | 1            |
|                            | Merchant   | 8     | 103      | 0.67(0.41–1.03) | 2.02(0.39–10.26)  |
|                            | Governmental | 0   | 20       | 0.49(0.11–1.92) | 0.43(0.11–1.60)   |
|                            | Non-governmental | 17 | 246     | 0.49(0.13–1.82) | 0.41(0.02–8.56)   |
| Presence of OIs            | Yes        | 10    | 203      | 4.14(1.68–5.23) | 4.58(1.20–5.65)*  |
|                            | No         | 29    | 268      | 1           | 1            |
| Place of residence         | Rural      | 15    | 136      | 1.71(0.95–2.43) | 0.42(0.09–1.92)   |
|                            | Urban      | 24    | 335      | 1           | 1            |
| Weight                     | < 60       | 35    | 358      | 2.38(1.87–9.32) | 2.48(1.59–10.38)* |
|                            | ≥60        | 4     | 113      | 1           | 1            |
| WHO clinical staging       | Stage I    | 6     | 188      | 1           | 1            |
|                            | Stage II   | 10    | 176      | 1.57(1.1–8.72)  | 2.14(0.40–11.29)  |
|                            | Stage III  | 11    | 70       | 3.73(2.2–4.68)  | 3.56(1.71–17.89)* |
|                            | Stage IV   | 12    | 37       | 10.29(1.93–21.13)| 4.42(1.75–25.93)* |

Abbreviations: CHR, crude hazard ratio; AHR, adjusted hazard ratio; CI, confidence interval; 1, reference category. *Statistically significant at p< 0.05; g/dl, gram per deciliter; OIs, opportunistic infections.
Data Sharing Statement
The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Ethical Consideration
Ethical clearance was obtained from the Tropical College of medicine ethical review committee (Reference: ERC/2129/ 2021). Letter of permission was obtained from Kombolcha town administration health office and consent was secured from each health centered. As the study was conducted through a review of medical records, obtain informed consent from patients’ was difficult. Data were extracted anonymously ensuring patient data confidentiality, and all data collection was conducted in compliance with the declaration of Helsinki.

Consent for Publication
Not applicable. No individual personal details, images, or videos are being used in this study.

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Author Contributions
All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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