

Survival and Its Determinants of HIV/AIDS Patients Receiving Antiretroviral Therapy in Two National Referral Hospitals in Eritrea: A Retrospective Cohort Study

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Introduction: HIV/AIDS continues to be a significant public health concern globally, particularly in low- and middle-income countries. In Eritrea, despite access to antiretroviral therapy (ART), many people living with HIV (PLHIV) continue to experience early mortality. Furthermore, survival analysis among those patients has not been conducted. Thus, this study aimed to assess the survival rates and identify the determinants of PLHIV on ART in two national referral hospitals in Eritrea.

Methods: A retrospective cohort study was used to recruit PLHIV aged 15 years or above who started ART between August 2005 and December 31, 2020, in Halibet National Referral Hospital (HNRH) and Orotta National Referral and Teaching Hospital. Data were extracted from a database and patients' medical records (patients' medical cards, laboratory results, and registries). The Kaplan–Meier estimator and the extended Cox proportional hazards regression were used for analysis.

Results: Of 3646 study participants, 11.5% died, 55.7% were on follow-up, 14.2% transferred out, and 18.5% lost to follow-up. The mortality rate was 1.32 per 100 person-years (95% CI: 1.20–1.44). Furthermore, by the end of the follow-up period, 79.7% of the patients survived. Of those who died, 70% and 60% survived their first and second year of ART initiation, respectively. Age above 45 years (HR=1.58, 95% CI: 1.05–2.37), ambulatory functional status (HR=2.49, 95% CI: 1.79–3.47), bedridden functional status (HR=2.88, 95% CI: 1.77–4.69), poor adherence (HR=1.57, 95% CI: 1.09–2.28), fair adherence (HR=2.19, 95% CI: 1.66–2.89) were predictors of poor survival. Conversely, CD4 count (cell/mm) 101–200 (HR=0.38, 95% CI: 0.25–0.55), 201–350 (HR=0.18, 95% CI: 0.11–0.27), above 350 (HR=0.05, 95% CI: 0.02–0.07), body weight 45–60 kg (HR=0.75, 95% CI: 0.59–0.94), weight above 60 kg (HR=0.53, 95% CI: 0.39–0.72), widowed (HR=0.49, 95% CI: 0.36–0.67), and residing outside Zoba Maekel (HR=0.53, 95% CI: 0.34–0.82) were predictors of good survival.

Conclusion: The mortality rate is relatively low. PLHIV who started ART above 45 years, bedridden and ambulatory, and those with poor adherence were more likely to have lower survival. HIV/AIDS control programs and other stakeholders are strongly recommended to strengthen community awareness of the importance of early testing, immediate initiation of ART, regular follow-up and treatment adherence.

Keywords: ART, determinants, Eritrea, HIV/AIDS patients, mortality rate, survival

Introduction

HIV/AIDS continues to be a public health concern globally, particularly in low- and middle-income countries. According to the Global Health Observatory, as of 2023, 39.9 million people were living with HIV, with 1.3 million new infections,

and 630,000 people died of AIDS-related illnesses.¹ The report also added that of all HIV-infected individuals, 38.6 million were adults, 1.4 million were children aged 0–14 years, and more than half (53%) were females. In 2023, the WHO Africa Region remained the most impacted by HIV/AIDS, accounting for approximately 65% of the global infection burden.² Treatment with combination antiretroviral therapy (ART) enables PLHIV to have prolonged and healthier lives. It also reduces their viral load significantly, which is essential in preventing onward transmission of HIV. In 2022, 76% of all HIV-positive individuals were accessing ART globally; moreover, countries in the African region reported that 90% of PLHIV knew their status, 82% were on treatment, and 76% had suppressed viral load.³

According to the UNAIDS report, in 2023, the number of adults and children living with HIV/AIDS in Eritrea was estimated at 13,000: 12,000 adults and 1000 children aged <15 years, where 8900 of them were under ART treatment.⁴ The report also estimated the annual number of deaths due to HIV/AIDS among adults was less than 500.

Several prospective and retrospective cohort studies have been conducted in different settings to investigate the survival and determinants of PLHIV after ART initiation. According to some studies, the overall mortality rate ranged from 2.03 to 4.18 per 100 person-years.^{5–8} In addition, several studies have reported high mortality of PLHIV in the first year of ART initiation.^{5,9,10} Moreover, various studies have documented the main predictors of survival of PLHIV on ART. Patients who started ART when their disease progression was advanced—at stage III or IV according to the WHO classification— or low baseline CD4 count were more likely to have shorter survival.^{5–7,10–12} Similar studies indicated that adherence was one of the main determinants of patients' survival.^{11,12} Besides, patients' survival was influenced by other factors such as sex, age, functional status, and anemia.^{5–8,10,12}

In situations where the key determinants for survival are not known, it is challenging to identify essential interventions and prioritize resources for the success of any HIV/AIDS control program. This study was therefore conducted to understand the survival of PLHIV on ART and explore its determinants for patients attending Halibet National Referral Hospital and Orotta National Referral and Teaching Hospital, located in Asmara, Eritrea.

Materials and Methods

Study Design and Setting

This retrospective cohort study enrolled PLHIV aged 15 years and above who started ART between August 2005 (ART was introduced in Eritrea in 2005) and December 31, 2020 and followed until December 31, 2021. The study was conducted in the HIV care clinics of Halibet National Referral Hospital (HNRH) and Orotta National Referral and Teaching Hospital (ONRTH). These HIV care clinics, based in the capital – Asmara, provide services to adults (15 years and above) and residents of the capital city and all regions of the country who decided to attend these sites for their reasons. These hospitals were selected because they are the only national referral hospitals that provide HIV care services in the country, and a significant proportion of PLHIV on ART received care in these hospitals. Of the 8775 PLHIV on ART in 2021, 2559 (29.2%) patients received treatment in these national referral hospitals.

Study Population

All PLHIV aged 15 years and above who were on ART between 2005 and December 31, 2021, and attending HIV care clinics at Halibet National Referral Hospital and Orotta National Referral and Teaching Hospital were eligible for enrollment. Patients who had missed information on outcome, date event (outcome) happened, and ART started date were excluded. In addition, PLHIV who re-restarted ART were excluded to minimize bias since their baseline information might differ from their measurement during the restart of ART. Patients who initiated antiretroviral therapy (ART) before age 15 were excluded from the study. This exclusion was necessary because these patients had initially received care at other pediatric clinics and were subsequently transferred to the participating hospitals, which do not provide ART to patients under 15 years of age.

Sampling Procedure and Power Calculation

The current study implemented a census (complete enumeration) of PLHIV attending the two national referral hospitals. Even though all patients registered in these HIV care clinics were enrolled, a power calculation was done to ensure that the sample size in the dataset provides sufficient power to investigate research question.¹³ Power was calculated based on two population proportion formulas. Functional status (working, ambulatory, or bedridden) of patients during ART initiation—one of the exposure variables—was believed to provide an optimal number. It was assessed using the Stata command for power calculation *stpower cox, n (133 38) hratio (2.49 2.88)* for the hazard ratio of ambulatory and bedridden, respectively. This command produced a power $\geq 90\%$. Thus, the study with the available number of patients had adequate power.

Data Sources

The primary data sources for this study were the existing electronic medical records and physically available medical cards of PLHIV. First, data were retrieved from the electronic medical records and exported to MS Excel Spreadsheet 2019. Information missing from electronic medical records—such as details found on patients' medical cards, laboratory results, and registries—was retrieved and manually entered into an MS Excel by data collectors.

Variables

Outcome Variable

The outcome variable was a pair of variables. One variable was an event-occurrence indicator, equal to 1 if death was known to occur and equal to 0 if death did not happen during the observation period (censored). Censored referred to patients who lost to follow-up, withdrew from treatment, transferred out, and were on follow-up at the end of the study period. The second variable was the time-to-event, which was the time from the start of ART to either the occurrence of death or censored.

Exposure Variables

The exposure variables were characteristics related to sociodemographic factors (age, sex, marital status, educational status, employment status, residence, and region), clinical conditions during ART debut (WHO clinical staging, CD 4 count, functional status, body weight), ART information (date of ART initiation), and follow up outcomes (adherence). The exposure variables were categorized as it is depicted in [Table S1](#). Moreover, the operational definitions of the variables considered in this study are provided in [Supplementary Information 1](#).

Data Management and Analysis

Data obtained from hospitals were exported to SPSS to be merged and cleaned; then, the dataset was exported to Stata version 13 for analysis. For categorical variables, data were presented as frequency and percent. Univariate and bivariate analyses were conducted based on all cases. However, missing values were dropped from the multivariate analysis; since they were small (3.3%), excluding them from the analysis was unlikely to introduce bias. Kaplan–Meier estimators and long-rank tests were used to assess the cumulative survival probability and survival curves. A hazard ratio with a 95% confidence interval and a two-sided chi-square significance test were used to measure the association between survival time and independent variables. Variables that were significant at a 0.2 significance level in the bivariate analysis were considered for the candidacy of the model building. Forward selection was used to select variables, and then multicollinearity was assessed. Moreover, the proportional hazard assumption was checked for every variable included in the model using Schoenfeld residual test and Schoenfeld scale. An extended Cox proportional hazards regression was used in multivariate analysis to identify the factors determining the survival time, as there were covariates that violated the proportional hazards assumption. P-value less than 0.05 was considered statistically significant.

Ethical Considerations

The Health Research Proposal and Ethical Committee of the Ministry of Health of Eritrea (reference number: 02/09/21) approved the study. In addition, permission was granted by the authorities of each ART care clinic to use the patients' information for the study. Due to the study's retrospective nature, the ethics committee waived the patient's consent.

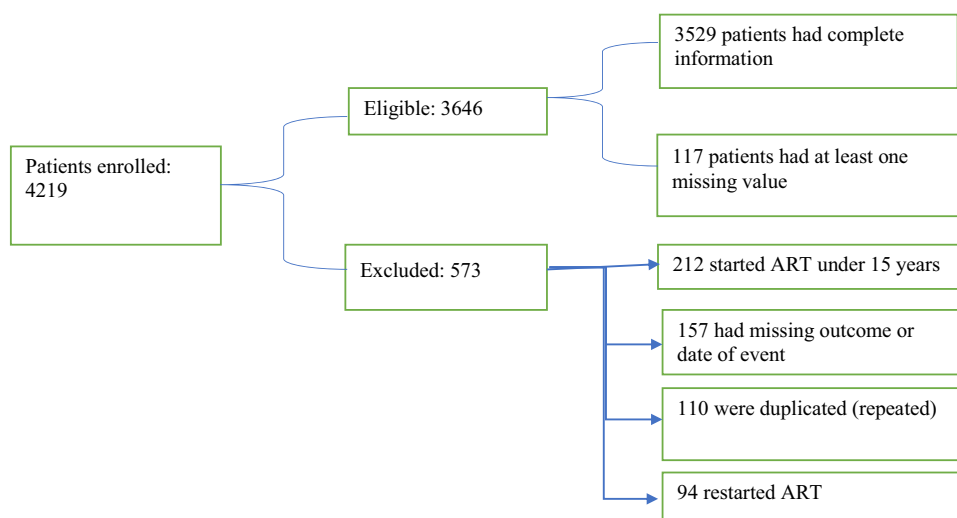


Figure 1 Summary of eligibility and enrollment of study participants who received antiretroviral therapy at Orotta National Referral and Teaching Hospital and Halibet National Referral Hospital followed up between 2005 and December 31, 2021 (N=3646).

However, the confidentiality of patients' data was ensured by coding their identifiers and removing them from the final analysis. In addition, data extraction was done by a staff working in the specific center to prevent external persons from accessing patient data. The study followed the Helsinki Declaration.

Results

Demographic, Clinical, and Laboratory Characteristics of Respondents

Overall, 4219 patients were assessed for eligibility, and 3646 (86.4%) were eligible for the study [Figure 1]. The median age of respondents was 36 years (Interquartile range [IQR]: 30–43). Sixty percent of the respondents were female, 58% were unemployed, and 48% were widowed. Over eight out of ten (84%) lived in urban areas, and 75% were from Zoba Maekel (central region). Most study participants (88%) had good adherence, and 56% were either in stage III or IV. Over a quarter (27%) started ART with a CD 4 count ≤ 200 cells/mm³, and 53% of respondents started ART with more than 350 cells/mm³. Most study participants (78%) started ART at working status, and 55% had a body weight between 45 and 60 kg (Table 1).

Table 1 Frequency and Mortality Rate of HIV/AIDS Patients Who Received Antiretroviral Therapy at Orotta National Referral and Teaching Hospital and Halibet National Referral Hospital Followed Up Between 2005 and December 31, 2021 (N=3646)

Variable		Number of Participants (%) ^a	Deaths	Person-Years at Risk	Mortality Rate per 100 Person-Years (95% CI)
Overall		3646 (100)	418	31,870.3	1.32 (1.20–1.44)
Sex	Male	1470 (40.32)	200	12,590.9	1.59 (1.39–1.83)
	Female	2176 (59.68)	218	19,279.5	1.14 (1.00–1.30)
Age	15-30	919 (25.21)	67	8194.1	0.82 (0.65–1.04)
	31-45	2099 (57.57)	230	18,785.7	1.23 (1.08–1.40)
	46 and above	628 (17.22)	121	4890.7	2.48 (2.08–2.96)
Employment status	Employed	1524 (42.1)	180	13,703.9	1.32 (1.14–1.53)
	Unemployed	2096 (57.9)	238	17,975.4	1.33 (1.17–1.51)

(Continued)

Table 1 (Continued).

Variable		Number of Participants (%) ^a	Deaths	Person-Years at Risk	Mortality Rate per 100 Person-Years (95% CI)
Educational status	No formal education	302 (8.37)	37	2602.3	1.43 (1.04–1.97)
	Primary	912 (25.26)	105	8843.6	1.19 (0.99–1.44)
	Secondary	2191 (60.69)	248	18,207.9	1.37 (1.21–1.55)
	Higher	205 (5.68)	23	2005.1	1.15 (0.77–1.73)
Marital status	Married	427 (11.76)	213	15,792.3	1.35 (1.18–1.55)
	Divorced/Sep	808 (22.25)	55	3445.9	1.60 (1.23–2.08)
	Single	652 (17.95)	97	6048.3	1.61 (1.32–1.96)
	Widowed	1745 (48.05)	52	6489.3	0.81 (0.62–1.06)
Region	Zoba Maekel	2715 (75.02)	349	23,611.6	1.48 (1.34–1.65)
	Outside Zoba Maekel	904 (24.98)	68	8102	0.84 (0.67–1.07)
Residence	Rural	579 (16)	62	5172.3	1.20 (0.94–1.54)
	Urban	3040 (84)	355	26,541.3	1.34 (1.21–1.49)
Baseline body weight(kg)	< 45	736 (20.2)	132	5117.7	2.58 (2.17–3.06)
	45-60	1996 (54.7)	215	17,349.6	1.24 (1.08–1.42)
	> 60	914 (25.1)	71	9403.1	0.76 (0.60–0.95)
Adherence	Good	3176 (87.4)	307	29,088	1.06 (0.95–1.19)
	Fair	306 (8.42)	76	1789.1	4.25 (3.4–5.32)
	Poor	152 (4.18)	35	879.8	3.98 (2.86–5.55)
Baseline WHO clinical stage	Stage I&II	1589 (43.64)	144	14,329	1.01 (0.86–1.19)
	Stage III&IV	2052 (56.36)	274	17,525	1.57 (1.39–1.77)
Baseline functional status	Working	2826 (77.62)	245	25,671	0.96 (0.85–1.09)
	Ambulatory	623 (17.11)	134	4472.9	3.00 (2.53–3.55)
	Bedridden	192 (5.27)	39	1710.6	2.29 (1.67–3.13)
Baseline CD 4 count	<=100	484 (13.29)	147	2254.3	6.53 (5.55–7.67)
	101-200	492 (13.51)	100	3303.4	3.03 (2.49–3.69)
	201-350	747 (20.52)	88	6325.9	1.40 (1.13–1.72)
	351 and above	1918 (52.68)	83	19,958	0.42 (0.34–0.52)

Note: ^a Discrepancy in number is due to missing values.

Mortality Rate

By the end of the study period, of those enrolled, 11.5% died, and 18.5% were lost-to-follow-up (Figure 2). The total observation time was 31870.3 person-years with a maximum observation time per person of around 17 years. The all-cause mortality rate was 1.32 per 100 person-years (95% CI: 1.20–1.44). The mortality rate was higher among those aged 46 years and above, males, divorced/separated, single, and patients living in Zoba Maekel. Mortality was also higher

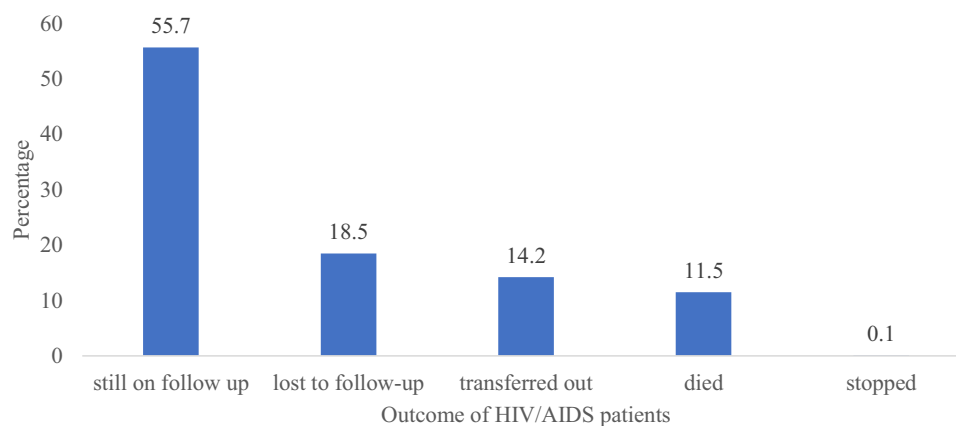


Figure 2 Follow-up outcome of HIV/AIDS patients who received antiretroviral therapy at Orotta National Referral and Teaching Hospital and Halibet National Referral Hospital followed up between 2005 and December 31, 2021 (N=3646).

among those who started ART with WHO clinical stages III and IV, those who were ambulatory or bedridden, had a CD 4 count of ≤ 200 cells/mm³ and had a body weight ≤ 45 kg as well as those with poor adherence (Table 1).

Survival Analysis

At the end of the study period, 79.7% of the study participants survived—with a survival probability of 0.80 (survivor function = 0.797, 95% CI: 0.766–0.825) (Figure 3 and Table 2). The median follow-up time was 9.15 years (IQR: 4.55–13.22 years). Of all participants, 96.4% survived their first year and 95.3% second year of ART initiation. Among those who died, 13%, 20%, and 30% died within three, six, and twelve months yielding a median survival time of 3.68 years (95% CI: 2.87–4.45). In addition, among those who died, 70% survived their first year and 60% survived their second year of ART initiation. The Kaplan-Meier curve indicated that the survival probability was lower for males, those aged 45 years and above, those who were married, divorced or separated, or single, and those who were residents of Zoba Maekel (Figure 4 and Table S1: Supplementary Information 1). Furthermore, patients with body weight of less than 45 kg, those who had fair or poor adherence, were on WHO clinical stages III and IV, had ambulatory or bedridden functional status, and those who had CD4 count ≤ 100 cells/mm³ during ART initiation had a lower survival probability (Figure 5 and Table S1: Supplementary Information 1).

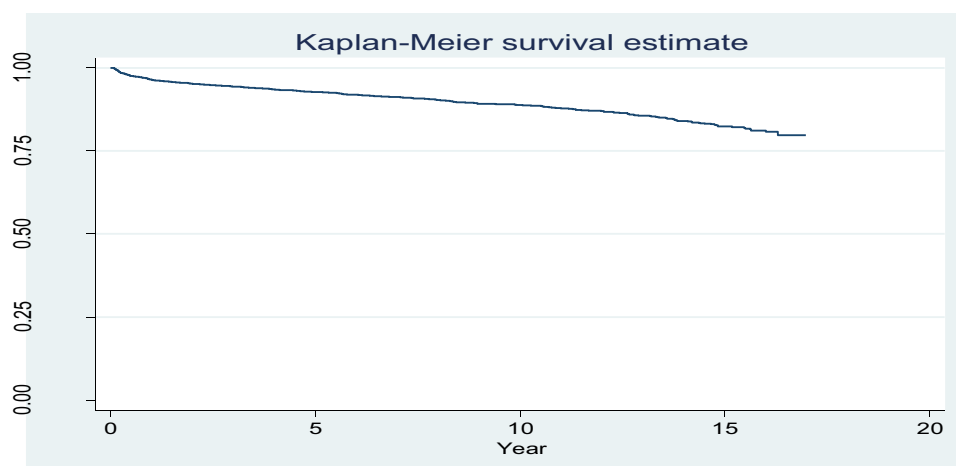


Figure 3 Kaplan-Meier survival estimate of patients who received antiretroviral therapy at Orotta National Referral and Teaching Hospital and Halibet National Referral Hospital followed up from 2005 to December 31, 2021 (N=3646).

Table 2 Survivor Function of Patients Who Received Antiretroviral Therapy at Orotta National Referral and Teaching Hospital and Halibet National Referral Hospital Followed Up Between 2005 and December 31, 2021 (N=3646)

Time (Years)	Beginning Total	Events	Survivor Function of Those Who Died (%)	Overall Survivor Function (%) (95% CI)
0.5	3423	86	79.43	97.59(97.04–98.05)
1	3316	41	69.62	96.41(95.74–96.98)
2	3120	39	60.29	95.25(94.49–95.91)
5	2643	77	41.87	92.75(91.82–93.59)
10	1641	93	19.62	88.88(87.67–89.97)
15	465	75	1.67	82.4(80.48–84.15)
16	194	6	0.24	80.74(78.37–82.88)
16.98	5	1	–	79.74(76.6–82.51)

Predictors of Survival

In bivariate analysis, sex, age, region, marital status, body weight, CD4 count, adherence, WHO clinical stage, and functional status at baseline were found to have a significant relationship with survival rates of PLHIV (Table 3). In multivariate analysis, patients who started ART above 45 years (HR=1.58, 95% CI: 1.05–2.37), who were ambulatory (HR=2.49, 95% CI: 1.79–3.47), or were bedridden (HR=2.88, 95% CI: 1.77–4.69), had poor adherence (HR=1.57, 95% CI: 1.09–2.28), or had fair adherence (HR=2.19, 95% CI: 1.66–2.89) had increased mortality. On the other hand, patients who started ART with a CD4 count (cells/mm³) of 101–200 (HR=0.38, 95% CI: 0.25–0.55), 201–350 (HR=0.18, 95% CI: 0.11–0.27), and over 350 (HR=0.05, 95% CI: 0.02–0.07), who had baseline body weight of 45–60 kg (HR=0.75, 95% CI: 0.59–0.94) and above 60 kg (HR=0.53, 95% CI: 0.39–0.72) had reduced mortality. In addition, those who were widowed (HR=0.49, 95% CI: 0.36–0.67) and those residing outside Zoba Maekel (HR=0.53, 95% CI: 0.34–0.82) had reduced mortality. The mortality risk also increased with age and treatment follow-up. Conversely, the disparities in mortality risk associated with regions, functional status, and CD4 count diminished with increased follow-up (Table 4).

Discussion

In this study, the mortality rate of PLHIV on ART was generally low. The excess mortality rate related to HIV/AIDS, however, could not be calculated as data on the mortality rate in the general population in Eritrea is unknown. The all-cause mortality rate of people living with HIV (PLHIV) on ART in Eritrea, without adjusting for the background mortality risk of the general population, was comparable to the excess mortality rate of HIV/AIDS reported in Luzhou, China (0.8 deaths per 100 person-years), suggesting a relatively low overall mortality rate.¹⁴ Besides, all-cause mortality reported in this study was almost similar to those reported in Tokyo, Japan (0.6 deaths/100 person-years).¹⁵

In the present study, a significant proportion of patients who started ART were lost to follow-up. However, this proportion was lower than that reported in studies conducted in Ethiopia (Benishangul-Gumuz), Sudan, and Kenya.^{16–18} Conversely, it was higher than the proportions reported in studies conducted in Uganda and eastern Ethiopia.^{19,20} The mortality rate of the present study was lower than the findings reported in India and a systematic review in sub-Saharan Africa.^{8,9,21} However, it was higher than the findings conducted in eastern and southern African countries.^{9,22} In this study, though it was difficult to identify HIV/AIDS-related deaths, as a cause of death was not well-documented in several patients, the majority of the all-cause deaths occurred in the first year of ART initiation, which is similar to findings reported elsewhere.^{5,9,10}

In this study, several sociodemographic and clinical characteristics were identified as determinants of survival: age, marital status, region, body weight, adherence, functional status, and CD4 count. Almost all are well-known risk factors for survival in PLHIV.^{6,21,23–26} This reflects that the time of initiation of ART and treatment adherence were the major

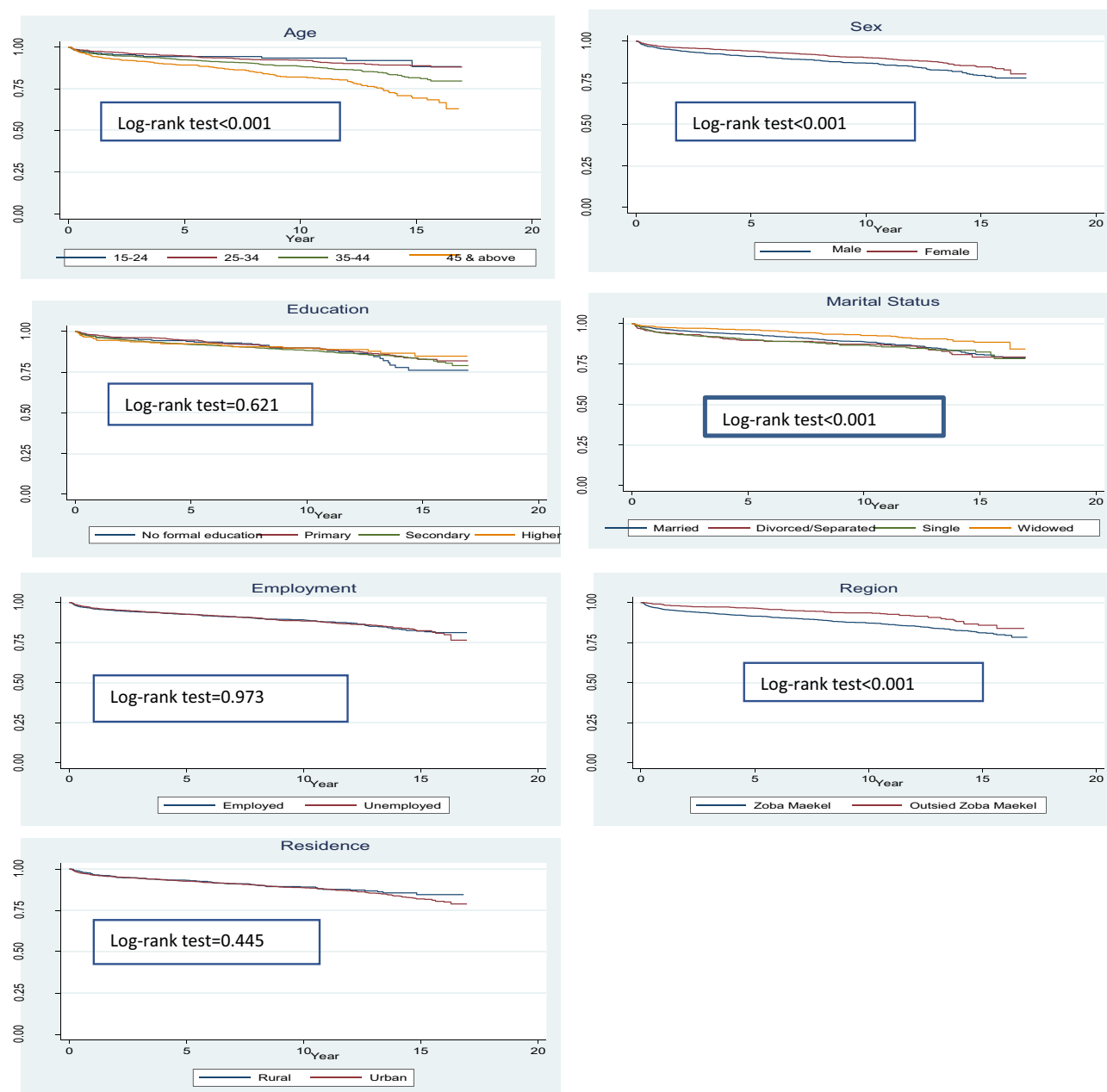


Figure 4 Kaplan-Meier survival estimates of HIV/AIDS patients who received antiretroviral therapy by sociodemographic characteristics at Orotta National Referral and Teaching Hospital and Halibet National Referral Hospital followed-up between 2005 and December 31, 2021 (N=3646).

modifiable determinants for improving survival. This is because early ART initiation with good treatment adherence can keep the immune system strong and help fight opportunistic infections that are among the common causes of death in PLHIV. This could ultimately improve body weight, patients' functionality, CD4 cell count, quality of life of PLHIV, prevent transmission of HIV, and suppress viral load, among others.^{24,25,27} A nationwide study in Eritrea that enrolled 6803 PLHIV confirmed that more than one-fourth (25.6%) of the study participants could not maintain their viral load to an undetectable level.²⁸ Coordinated efforts should be made to maximize the proportion of PLHIV with undetectable viral load count to cut the transmission cycle of HIV and ultimately achieve one of the three 95s of the 2025 AIDS Targets: 95% achieving suppression of their viral load.^{29,30}

The study's findings have several clinical, programmatic, and policy implications. First, only a few patients have died while on treatment, and the majority of them were those who started their treatment late and during the first year of ART

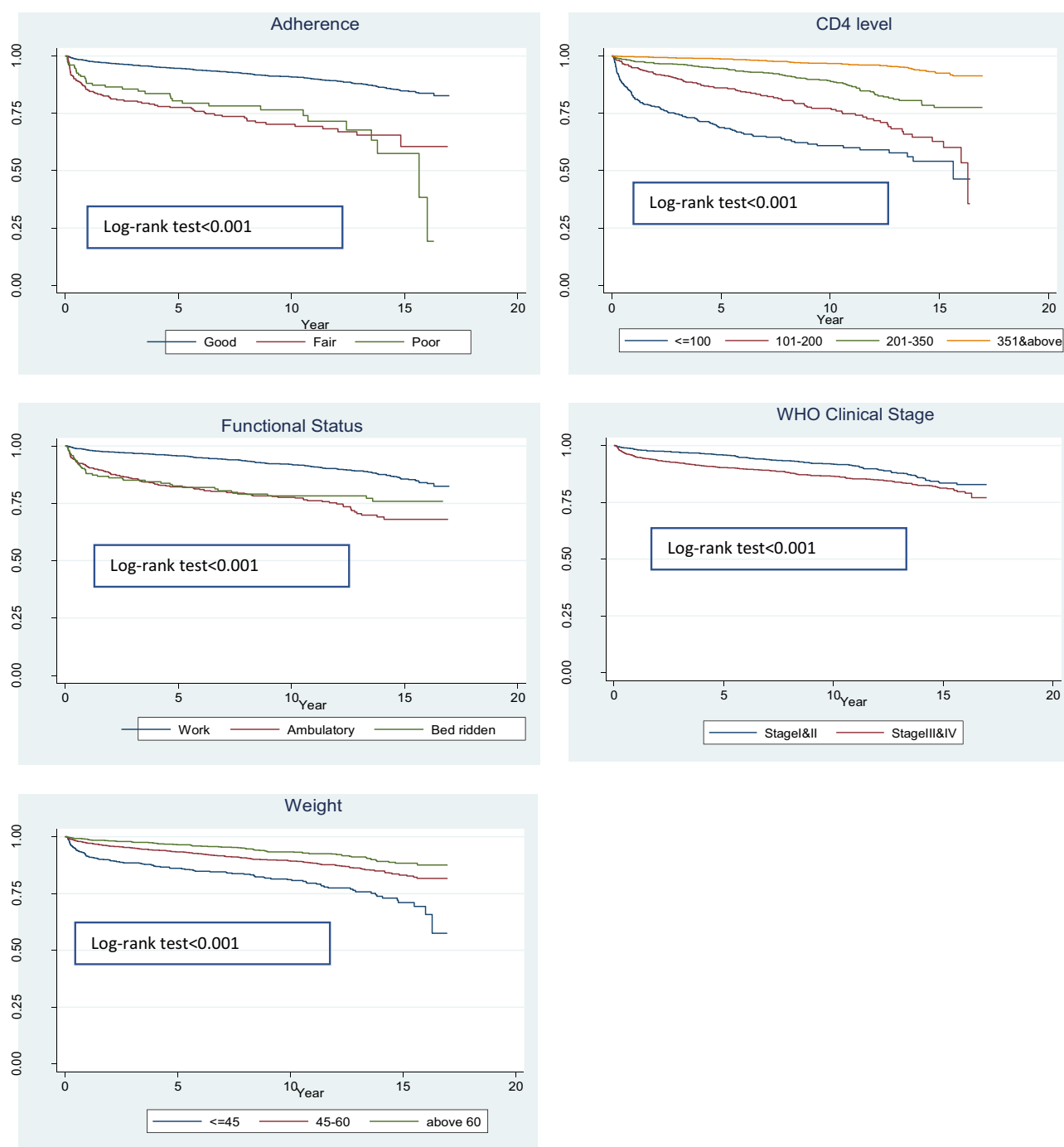


Figure 5 Kaplan-Meier survival estimates by laboratory and clinical characteristics of HIV/AIDS patients who received antiretroviral therapy at Orotta National Referral and Teaching Hospital and Halibet National Referral Hospital followed up between 2005 and December 31, 2021 (N=3646).

initiation. Thus, practitioners and the program should look at mechanisms that enhance early treatment-seeking behavior as well as care during the first year of treatment debut. Second, the National HIV/AIDS Control Program needs to identify mechanisms for the death audit of PLHIV and tracing lost-to-follow-up cases. Otherwise, it is difficult to know precisely HIV/AIDS-related mortality as, for several patients, the cause of death could not be qualified. Knowing the HIV/AIDS-related deaths would help the National HIV/AIDS Control Program in evaluating its performance. Third, individual, societal, and programmatic drivers/barriers that could affect knowing their HIV/AIDS status, early initiation of ART, and treatment adherence should be identified, and appropriate risk management plans need to be implemented.

Table 3 Bivariate Analysis of Patients Who Received Antiretroviral Therapy at Orotta National Referral and Teaching Hospital and Halibet National Referral Hospital Followed Up Between 2005 and December 31, 2021 (N=3646)

Variable		Hazard Ratio (95% CI) ^a	p-value ^b
Age	15-30	1	
	31-45	1.51 (1.15–1.97)	0.003
	46 and above	2.96 (2.2–3.99)	<0.001
Sex	Male	1	
	Female	0.72 (0.6–0.88)	0.001
Employment status	Employed	1	
	Unemployed	1.01 (0.83–1.22)	0.973
Educational status	No formal education	1	
	Primary	0.84 (0.58–1.22)	0.355
	Secondary	0.95 (0.67–1.34)	0.754
	Higher	0.81 (0.48–1.36)	0.41
Marital Status	Married	1	
	Divorced/Separated	1.17 (0.87–1.57)	0.314
	Single	1.17 (0.92–1.48)	0.225
	Widowed	0.60 (0.45–0.82)	0.001
Region	Zoba Maekel	1	
	Outside Zoba Maekel	0.57 (0.44–0.74)	<0.001
Residence	Rural	1	
	Urban	1.12 (0.85–1.46)	0.445
Baseline body weight(kg)	<45	1	
	45-60	0.50 (0.41–0.62)	<0.001
	Above 60	0.31 (0.24–0.42)	<0.001
Baseline CD 4 count (cells/mm ³)	≤100	1	
	101-200	0.49 (0.38–0.63)	<0.001
	201-350	0.23 (0.18–0.3)	<0.001
	351 and above	0.07 (0.06–0.09)	<0.001
Adherence	Good	1	
	Fair	3.86 (3–4.96)	<0.001
	Poor	3.56 (2.51–5.05)	<0.001
Baseline WHO clinical stage	Stage I&II	1	
	Stage III&IV	1.54 (1.26–1.89)	<0.001

(Continued)

Table 3 (Continued).

Variable		Hazard Ratio (95% CI) ^a	p-value ^b
Baseline function status	Working	1	
	Ambulatory	3.08 (2.49–3.8)	<0.001
	Bedridden	2.37 (1.69–3.32)	<0.001

Notes: ^a Hazard ratio 1 refers to the reference group; ^b p-value from Wald test.

Abbreviation: CI, confidence interval.

Table 4 Multivariate Analysis Patients Who Received Antiretroviral Therapy at Orotta National Referral and Teaching Hospital and Halibet National Referral Hospital Followed Up Between 2005 and December 31, 2021 (N=3529)

Variables		Hazard Ratio (95% CI) ^a	P-value ^b
Main			
Age group	15-30	1	
	31-45	1.11 (0.8–1.53)	0.545
	46 and above	1.58 (1.05–2.37)	0.029
Region	Zoba Maekel	1	
	Outside Zoba Maekel	0.53 (0.34–0.82)	0.004
Baseline CD 4 count (cells/mm3)	≤100	1	
	101-200	0.38 (0.25–0.55)	<0.001
	201-350	0.18 (0.11–0.27)	<0.001
	Above 350	0.05 (0.02–0.07)	<0.001
Baseline functional status	Working	1	
	Ambulatory	2.49 (1.79–3.47)	<0.001
	Bedridden	2.88 (1.77–4.69)	<0.001
Baseline body weight	<45	1	
	45-60	0.75 (0.59–0.94)	0.011
	Above 60	0.53 (0.39–0.72)	<0.001
Adherence	Good	1	
	Fair	2.19 (1.66–2.89)	<0.001
	Poor	1.57 (1.09–2.28)	0.018
Marital status	Married		
	Divorced/Separated	0.94 (0.7–1.27)	0.686
	Single	0.90 (0.7–1.16)	0.38
	Widowed	0.49 (0.36–0.67)	<0.001

(Continued)

Table 4 (Continued).

Variables		Hazard Ratio (95% CI) ^a	P-value ^b
TVC (Time-varying covariate)			
	Age_31-45*time	1.01 (1.00–1.02)	0.096
	Age_46 and above*time	1.02 (1.01–1.03)	0.028
	Outside Zoba Maekel*time	1.01 (1.01–1.02)	0.024
	101-200*time	1.02 (1.01–1.02)	<0.001
	201-350*time	1.02 (1.01–1.02)	<0.001
	Above 350*time	1.02 (1.01–1.03)	<0.001
	Ambulatory*time	0.99 (0.99–0.99)	0.005
	Bed ridden*time	0.99 (0.98–0.99)	0.002

Notes: ^a Hazard ratio 1 refers to the reference group. ^b P-value from Wald test.

Abbreviation: CI, confidence interval.

The National HIV/AIDS Control Program should enhance adherence, retention, and re-engagement support to improve treatment adherence among patients. This will ultimately help the country to achieve the globally set “95–95–95” AIDS targets at a reasonable time. Besides, this could prevent/minimize treatment failure and drug resistance. Fourth, in the current study, a significant number of participants attending the HIV care clinics of the national referral hospitals were coming from other zobas despite the availability of nearby ART sites. They might have opted to receive their treatment in a distant area, possibly due to concerns of disclosing their HIV/AIDS status to their community for fear of stigma and discrimination. Fear of stigma and discrimination not only discourages patients from being enrolled at a nearby HIV care clinic, but it could also increase reluctance to know their HIV status. The National HIV/AIDS Control Program should, therefore, identify barriers to getting services from nearby clinics, and a well-thought-out plan should be developed and implemented in a coordinated fashion. Furthermore, the National HIV/AIDS Control Program should enhance psychological support services for patients, enabling them to effectively cope with stigma and discrimination.

The present study benefited from having adequate power (more than 90%)—the sample size was large as all eligible individuals in the national referral hospitals were considered. Moreover, the study had a long follow-up time, with a maximum of 17 years. However, the study had several limitations. This study used secondary data extracted from the ART follow-up database in the HIV care clinics of the national referral hospitals, and patient cards were reviewed to record missing values in the database. This resulted in missing information for some variables and characteristics that might have affected a patient’s survival. Furthermore, all-cause mortality was considered—as HIV/AIDS-related deaths were not well documented—and this could have overestimated the mortality rate of HIV/AIDS patients. In addition, since adherence was repeatedly taken during follow-ups, the most frequently reported value was considered. Finally, the result could not be generalized to patients who took ART treatment at other HIV care clinics, patients who started ART before the age of 15, and those who restarted ART at the study sites. In the future, a prospective cohort study should be conducted that addresses the limitations of the present study. In addition, qualitative research that could help understand why people initiate ART late and factors that affect adherence need to be uncovered. Furthermore, the quality of life of HIV/AIDS patients who receive ART should also be investigated.

Conclusions

This study investigated the survival status of patients receiving ART and identified significant determinants that affect their survival. Overall, all-cause mortality among PLHIV was relatively low compared to similar studies conducted in other settings. However, a substantial proportion of patients lost their follow-up appointments. Furthermore, more than three-fourths of the patients survived by the end of the study period, although most of the deaths occurred during the

first year of ART initiation. The present study indicated that patients who started ART over the age of 45 were more likely to experience shortened survival. Additionally, starting ART at an advanced clinical stage (ambulatory or bed-ridden) and having poor to fair treatment adherence were identified as the significant modifiable determinants of survival. The fact that most of the deaths occurred during the first year of ART initiation reflects the need for early treatment-seeking behavior. Thus, it is important to stress patient education that focuses on early treatment, regular follow-up, and adherence to treatment to enhance the HIV/AIDS control strategies. In addition, the HIV/AIDS program should conduct an operational study to understand the barriers that hinder early ART initiation.

Compliance with Ethics Guidelines

The research was approved by the Health Research Proposal and Ethical Committee of the Ministry of Health of Eritrea (reference number 02/09/21). Besides, the authorities of each ART care site were asked for permission to use the patient's information for the study. Due to the retrospective nature of the study, the ethics committee waived the patient's consent. However, the confidentiality of patients' data was ensured by coding their identifiers and removing them from the final analysis. In addition, data extraction was done by a staff working in the specific center to prevent external persons from accessing patient data. The study followed the Helsinki Declaration.

Data Sharing Statement

All data generated or analyzed during this study are included in this published article/as supplementary information files.

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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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Disclosure

The authors declare that they do not have a conflict of interest in this work.

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