

Time to initiation of antiretroviral therapy and its predictors among newly diagnosed HIV positive at the selected public health centers in Adama Town, Ethiopia



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Abstract

Introduction Antiretroviral therapy (ART) has significantly reduced HIV infections, but late initiation remains a major issue. This study aimed to identify predictors of ART initiation among newly diagnosed HIV-positive patients in Adama town.

Method A retrospective cohort study was conducted, with 396 newly diagnosed HIV-positive patients. This study used a survival analysis approach, including Kaplan-Meier plots, the log-rank test, and the Cox proportional hazards model.

Result The incidence rate was 152 per 1000 person-days for early initiation after HIV positive confirmed. In the adjusted model, gender, VCT test, disclosure status, having children in the home, opportunistic infections, and HIV/TB co-infections were significantly associated with time to ART initiation.

Conclusion To enhance early ART initiation, healthcare programs should prioritize support for women patients, promote HIV serostatus disclosure, and improve access to VCT testing. Targeted interventions for those with comorbidities and support for families with children are also essential.

Keywords ART initiation, Exposure, People living with HIV, Survival analysis, Ethiopia

Introduction

Globally, 29.8 million HIV-positive patients had access to antiretroviral therapy (ART) [1, 2], contributing to a nearly 30% reduction in new HIV infections and a 42% reduction in HIV-related mortality [3]. Oguntibeju et al. (2012) [4] and Aranda-Naranjo et al. (2004) [5] have provided evidence that has given hope to people living with

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mortality, higher healthcare costs, poor retention in care, and inadequate viral suppression [11, 14].

Ethiopia has integrated the Universal Test and Treat (UTT) strategy into its national policy since 2016, and the current ART guidelines are followed and implemented accordingly [15]. It recommends that all individuals with confirmed HIV infection start ART immediately or within 7 days [16-19], regardless of the patient's WHO clinical stage or CD4+count [20]. Since the prevalence of HIV in Ethiopia remains high [16, 19, 21], it is crucial to revitalize and scale up HIV prevention and intervention [22-25]. Early ART initiation following HIV infection facilitates rapid viral suppression, reduces mortality and morbidity, and improves disease prognosis [23, 26, 27]. However, many HIV-positive patients in lowand middle-income countries face challenges with timely ART initiation [9]. In Ethiopia, there is limited information on the time taken to start ART for newly diagnosed HIV-positive individuals. This study aims to address this gap by estimating the time from HIV diagnosis to ART initiation and identifying predictor variables.

Table 1	Socio-demographic characteristics of newly diagnosed
HIV-posit	tive patients in Adama town, Ethiopia, 2023

Variables	Frequency	Percent (%)		
Age (n, %)				
15–24	65	16.4		
25–34	139	35.1		
>35	192	48.5		
Women participants (n, %)	241	60.9		
Pregnancy mother (n, %)	225	94.6		
Marital status (n, %)				
Single	87	22		
Married	195	49.2		
Divorced	71	17.9		
Widowed	43	10.9		
Education status (n, %)				
No primary	72	18.2		
Primary	168	42.4		
Secondary	124	31.3		
Higher	32	8.1		
Religion of participants (n, %)				
Orthodox	240	60.6		
Muslim	86	21.7		
Protestant	65	16.4		
Others	5	1.3		
Employment status (n, %)				
Governmental	21	5.3		
Self-employed	218	55.1		
Unemployed	157	39.6		

Methods

Study setting and design

A retrospective cohort study was conducted from March 1 to April 12, 2023, at selected health facilities in Adama Town, located in the East Shewa Zone, 99 km southeast of Addis Ababa. Adama, nestled between an escarpment to the west and the Great Rift Valley to the east, has an estimated population of 467,231. The population are engaged in farming, focusing on crops, livestock, trade and merchant activities. Twenty-one health centers in Adama town offer HIV testing services, and approximately 14,001 people are currently receiving antiretroviral therapy (ART) in the town. The health centers offer a variety of service levels, enabling them to address a broad spectrum of patient needs, from routine care to specialized medical treatments. This comprehensive approach supports the effective initiation and management of ART.

Inclusion and exclusion criteria

The study included all newly diagnosed HIV-positive individuals aged 15 and above at selected public health centers who underwent HIV testing between September 1, 2017, and December 30, 2021. Individuals with incomplete data, such as missing records of the HIV diagnosis date or ART initiation date, were excluded from the study.

Sample size and sampling procedure

To determine the sample size for survival data, the logrank method was employed, considering the study's power and hazard ratio (HR). This method assumes proportional hazards and adjusts for the withdrawal rate, ensuring the log-rank value aligns with the event rate at the study's conclusion. STATA version 17 was used to calculate the probability of events and survival functions at $(S_1)t$ and $(S_2)t$. The analysis assumed a 0.5 probability of the event, a 10% withdrawal probability, and HRs derived from a previous study on ART initiation predictors among people living with HIV in Ethiopia [19]. The hazard ratios (HRs) of predictors such as educational level, gender, and the presence of opportunistic infections (OIs) were used to determine the sample size. Among these predictors, educational level yielded the largest sample size of 399.

Three health facilities were included to select newly diagnosed HIV-positive patients from September 1, 2017, to August 30, 2021. Using proportional allocation, the required sample sizes were generated from each health center based on a computer-based simple random sampling technique.

Data collection and quality control

Data were collected using a checklist developed in English. This form was created based on HIV testing and counseling services logbooks, ART intake forms, and HIV care follow-up records, and it was further refined using insights from various peer-reviewed published studies [19, 21, 28]. Data were collected by two trained clinical nurses under the supervision of a nurse with a Bachelor of Science (BSc). The overall process was overseen by the study's principal investigator. Data collectors and supervisors received one day of training on the study's purpose, tools, data collection procedures, and data handling. The data collectors reviewed data completeness, and the data were checked daily for clarity and consistency.

Study variables and measurements

The dependent variable in this study was the time to initiation of ART. The independent variables included several socio-demographic characteristics, such as gender, age at HIV diagnosis, marital status, occupational status, educational level, religion, and residence; clinical characteristics, including the WHO stage of disease progression, CD4 count, baseline opportunistic infections (OIs), baseline comorbidity, TB screening, and TB/HIV co-infection; the HIV test approach; and personal and family factors, such as disclosure status, partner HIV status, provider-initiated counseling and testing (PICT), and voluntary counseling and testing (VCT).

Data analysis

Descriptive statistics, including the median with interquartile range, frequencies, and proportions, were used in this study. Time to ART initiation was estimated using the Kaplan-Meier method, and the log-rank test was applied to compare survival times between groups of categorical variables. A bivariate and multivariable Cox proportional hazards regression model was used to identify predictors of ART initiation while controlling for confounding factors. In this study, the forward variable selection method was used for model building. Graphical methods were employed to check the Cox proportional hazards assumption, and multicollinearity was assessed using the variance inflation factor (VIF = 1.18), indicating the absence of multicollinearity effects. The model's overall goodness of fit was evaluated using the Cox-Snell residual plot. Adjusted hazard ratios (AHR) with 95% confidence intervals (CIs) and p < 0.05 were used to determine the strength of the association. All analyses were performed using the R program.

Ethical statements

Ethics approval was obtained from the Institutional Ethical Review Board (IERB) of Adama Hospital Medical College, with reference number 0996/k-373/15. The study ensured that all information was kept confidential throughout the research process.

Table 2	Baselii	ne clinica	al related	characte	eristics	of nev	wly	
diagnose	ed HIV	positive _l	patient ir	1 Adama	town,	Ethiop	oia,	2023

Variables	Frequency	Percent (%)
BMI (n, %)		
Underweight	58	14.6
Healthy weight	315	79.5
Overweight	23	5.8
Viral Load > 1000 copies/mL (n, %)	61	15.4
Baseline CD4 count < 500 cell/mm ³ (n, %)	266	67.2
WHO stage (n, %)		
Stage I	285	72
Stage II	78	19.7
Stage III	31	7.8
Stage IV	2	0.5
Baseline opportunistic infections (n, %)	67	16.9
Baseline comorbidities (n, %)	6	1.5
HIV-TB co-infection (n, %)	14	3.5
Who have children < 15 years (n, %)	234	59.1
Children with HIV positive (n, %)	6	2.6
Functional status (n, %)		
Working	375	94.7
Ambulatory	15	3.8
Bedridden	6	1.5
VCT test approach (n, %)	261	66
HIV result disclosed (n, %)	297	75
Partners' HIV positive (n, %)	183	48.9
To whom HIV results disclosed (n, %)		
Spouse	132	44.4
Siblings	43	14.5
Own child	18	7.7

BMI: body mass index; WHO; world health organization;

Results

Socio-demographic characteristics of the participants

A total of 399 newly diagnosed HIV-positive patients were included in this study. The median age of the participants was 34 years [IQR: 26–41]. Among them, 331 (83.6%) were 24 years old or older. Of the total, 241 (60.9%) were women. Additionally, 195 (49.2%) participants were married, and 168 (42.4%) had attended primary school. In this study, 240 (60.6%) participants were Orthodox followers, and 218 (55.1%) were self-employed (Table 1).

Clinical and facility-related characteristics

The median BMI of participants was 21.3 [IQR: 19.5–23.1]. Two hundred sixty-six (67.2%) participants had a CD4 cell count of <500 cells/mm³, 285 (72%) participants were classified as stage I, and 375 (94.7%) had a working functional status. The majority of participants, 329 (83.1%), had no opportunistic infections (OIs), 382 (96.5%) had no TB/HIV co-infection, and 390 (98.5%) had no comorbidities. Two hundred thirty-four (59.1%) participants had children under 15 years old, and 261 (66%) were tested for HIV using the VCT approach.



Treatment started Transferred out Lost to followuup

Fig. 1 Test outcome of newly diagnosed HIV-positive patient in Adama town, Ethiopia, 2023

Accordingly, 297 (75%) disclosed their HIV status, and 132 (44.4%) disclosed to their spouse (Table 2).

Incidence and time to ART initiation

The overall incidence rate of ART initiation was 152 (95% CI: 136–169) per 1,000 person-days, and the median time to ART initiation for newly diagnosed HIV-positive individuals was 1 day [IQR: 1–9]. In this study, 322 newly diagnosed HIV-positive patients (81.31%; 95% CI: 0.77–0.85) initiated ART during the follow-up period (Fig. 1). Two hundred eighty-eight (89%; 95% CI: 0.86–0.93) initiated ART within 7 days of a confirmed positive HIV diagnosis and 201 (69.8%) of them started ART on the same day their HIV diagnosis was confirmed. Of the total newly confirmed cases, 17.4% were transferred to other health facilities during the follow-up period.

Survival pattern

Based on the Kaplan-Meier survival curve, there is a significant difference in the time to initiation of ART among gender, baseline opportunistic infections, HIV/ TB co-infection, testing approach, HIV disclosure status, and those who had children under 15 years (all p < 0.001, Figs. 2, 3, 4, 5, 6 and 7), respectively.

Predictors of time to ART initiation among newly HIV diagnosed

In the multivariable Cox proportional hazards regression model, the predictors significantly associated with ART initiation at the 5% level of significance included gender, the presence of opportunistic infections (OIs), HIV testing approach, HIV disclosure status, HIV/TB co-infection, and having children under 15 years old.



Fig. 2 The Kaplan-Meier curve with the number at risk illustrates the survival differences between men and women patients

Women participants had a 30% higher likelihood of timely ART initiation compared to males (adjusted hazard ratio [AHR]: 1.30; 95% confidence interval [CI]: 1.02– 1.65). Participants with baseline opportunistic infections (OIs) had a 31% lower likelihood of timely ART initiation compared to those without OIs (AHR: 0.69; 95% CI: 0.49–0.97). The hazard of timely initiating ART was 1.82 times higher for those who were tested for HIV via the VCT approach compared to those tested using the PITC approach (AHR: 1.82; 95% CI: 1.03–3.22). The hazard of timely initiating ART was 1.32 times higher for individuals who disclosed their HIV status compared to those who did not disclose their status (AHR: 1.32; 95% CI: 1.00–1.73). The hazard of timely initiating ART for those with children was 1.61 times higher than for participants without children (AHR: 1.61; 95% CI: 1.24–2.10). Participants with HIV/TB co-infection had a 66% lower likelihood of timely ART initiation compared to their counterparts (AHR: 0.34; 95% CI: 0.12–0.93) (Table 3).



Fig. 3 Kaplan-Meier curve with the number at risk, showing the survival difference between individuals who have disclosed diagnostic results and those who have not

Discussion

This study found that 81% of newly diagnosed HIV-positive individuals initiated ART, consistent with a previous Sub-Saharan Africa study reporting 84% ART initiation [29]. However, it is higher than the findings of a study conducted in Ethiopia (71.6%) [19] but lower than the 96% reported in a study conducted in South Africa [30]. The differences in ART initiation rates may be due to variations in treatment guidelines across countries, differences in study durations, increased service accessibility, and variability in socio-demographic characteristics among the populations studied.



Fig. 4 Kaplan-Meier curve with the number at risk shows the survival differences between respondents tested through PICT and VCT approaches

On the other hand, the results of this study reveal that 89.4% of participants-initiated ART within 7 days of a confirmed HIV-positive diagnosis. This result is higher than those of studies from Nekemte Town in Ethiopia and eThekwini Clinics in KwaZulu-Natal, South Africa,

where immediate ART initiation rates were 67.4% and 79%, respectively [30]. The observed difference could be attributed to variations in healthcare infrastructure, as the current study was conducted in the second largest city of Ethiopia, compared to Nekemte and a small facility



Fig. 5 The Kaplan-Meier curve shows the survival difference between individuals with baseline opportunistic infections and those without opportunistic infections

study conducted in eThekwini Clinics in KwaZulu-Natal, South Africa. Differences in access to ART services and program implementation strategies may also play a role. Additionally, increased awareness, enhanced diagnostic tools, and streamlined ART initiation protocols in recent years may have contributed to the higher rates observed in this study compared to earlier studies. However, the uptake of immediate ART initiation in this study was lower than a similar study in Cameroon, which reported a rate of 94.9% [19, 31]. Additionally, while 76.8% of clients in Cameroon initiated ART on the same day as their HIV diagnosis [31], this was slightly higher than the 69.8% observed in the current study. The inconsistency may due to differences in the study period and setting, as this study focused solely on health centers, while previous studies included both hospitals and health centers, potentially explaining the variation in findings.

We found that the overall median time to ART initiation was 1 day [IQR: 1-9]. This aligns with evidence from a review on rapid ART initiation, which showed that newly diagnosed HIV-positive individuals, on average, started ART within 7 days of receiving a confirmed diagnosis [2]. The findings are in agreement with a study conducted in Cameroon [31] and Nekemte town [19] that reported the median time to ART initiation was 1.61, and 4 days, respectively. In contrast, the current findings showed a shorter time for ART initiation compared to those reported in other studies: 16 days in Zimbabwe [32], 20 days in Portugal [1], 40 days in Myanmar [33], 58 days in Malawi [34], and 71 days in New York City [35]. The discrepancies may be due to differences in treatment guidelines for ART initiation. In earlier studies, CD4 cell count and WHO clinical stage were used as eligibility criteria for starting ART, often leading to delays in treatment. However, under the current 'treat-all' approach, all

Fig. 6 The Kaplan-Meier curve with the number at risk shows the survival difference between individuals with and without HIV/TB co-infections

individuals with a confirmed HIV diagnosis are started on ART immediately, regardless of their CD4 count or clinical stage, which likely accounts for the shorter time to ART initiation.

This study found that the time to ART initiation was shorter for women. This finding is consistent with study results from Northern Ethiopia [20], Nekemte town [19], Cameroon [31], and Haiti [28]. However, this finding contrasts with studies conducted in New York City [35] and Mozambique [36], which reported that women experienced delays in ART initiation compared to men. The earlier initiation of ART among women in this study may be due to their more frequent engagement with the healthcare system, particularly through antenatal and postnatal care and family planning services, where prevention of mother-to-child transmission (PMTCT) programs are emphasized. On the other hand, the delays may be partly due to the predominantly women-oriented nature of many HIV care clinics, which could unintentionally create an environment that feels less accessible or welcoming to men.

In this study, we observed that individuals tested for HIV using the VCT approach-initiated ART more quickly than those tested through the PITC method. This finding aligns with previous research conducted in Ethiopia, indicating the effectiveness of VCT in facilitating timely ART initiation [11, 19]. Individuals tested through VCT generally receive more comprehensive information about risky behaviors, ART initiation, and preventing onward transmission compared to those tested via PITC. This enhanced awareness may contribute to the earlier initiation of ART.

This study found that individuals who disclosed their HIV-positive status-initiated ART earlier than those who did not. Disclosure can help individuals build selfconfidence, reduce HIV-related stigma, and gain social support from relatives and friends, all of which encourage earlier ART initiation. This finding is consistent with previous studies conducted in Ethiopia [21] and Nekemte town [19], which reported that people living with HIV who disclosed their status started ART earlier than those who chose not to disclose.

Fig. 7 The Kaplan-Meier curve with the number at risk shows the survival difference between respondents who have children under 15 years and those who do not

This study found that HIV-positive individuals with children in their households-initiated ART more promptly than those without children. This may be due to the more frequent contact these patients have with the healthcare system, where they receive crucial information about the importance of early ART initiation to reduce mother-to-child transmission (MTCT). This result aligns with findings from other studies conducted in Africa [37].

We found that individuals with baseline opportunistic infections (OIs) and those with HIV/TB co-infection experienced longer times to ART initiation compared to their counterparts. This finding is supported by studies conducted in Nekemte town [19], Cameroon [31], Northern West Ethiopia [20], and the WHO report [2]. The delay in ART initiation among people with baseline OIs may be due to concerns about immune reconstitution inflammatory syndrome (IRIS), which can occur when immune-suppressed individuals begin HIV treatment. For those with HIV/TB co-infection, the delay might be attributed to fears of drug-drug interactions and toxicities associated with simultaneously treating HIV and a chronic disease.

This study has some limitations. These findings may not be generalizable to the entire population, as they exclude data on infants and children. Therefore, they should be used with caution as evidence at a similar facility level. Second, some patients were transferred before **Table 3** Bivariable and multivariable Cox proportional hazard model time to ART initiation and its predictors among newly diagnosed HIV positive patients in Adama ton, Ethiopia, 2023

Variables	Category	Survival Status		CHR	AHR	P-value	
		Event (ART initiated)	Censored				
Gender	Men	115	40	1	1		
	Women	207	34	1.37(1.10-1.74)	1.30(1.02-1.65)	0.035 *	
Baseline Ols	No	282	47	1	1		
	Yes	27	40	0.55(0.39–0.77)	0.69(0.49–0.97)	0.031*	
Baseline co-morbidities	No	321	69	1	1		
	Yes	1	5	0.12(0.02-0.83)	0.14(0.02-1.00)	0.05	
Test approach	PICT	92	43	1	1		
	VCT	230	31	1.49(1.17-1.90)	1.82(1.03-3.22)	0.041*	
HIV/TB co-infection	No	318	64	1	1		
	Yes	4	10	0.23(0.08-0.57)	0.34(0.12-0.93)	0.036 *	
Disclosure status	No	70	39	1	1		
	Yes	252	45	1.43(1.10-1.87)	1.32(1.00-1.73)	0.048 *	
Presence of children	No	108	54	1	1		
	Yes	214	20	1.81(1.43-2.29)	1.61(1.24–2.10)	< 0.001 *	

Ols: opportunistic infections; CHR: crude hazard ratio; AHR: adjusted hazard ratio; PICT: provider-initiated counselling and testing; VCT: voluntary counseling and testing; OPD: outpatient department; HIV: human immunodeficiency virus; TB: tuberculosis; * indicates a statistically significant

ART initiation, leaving their outcomes unknown. As a result, the estimate may be slightly affected. Thirdly, this study did not assess the distribution of healthcare professionals working in ART clinics, making it impossible to quantify gender-based influences on patients' early or late ART initiation. Further qualitative research is warranted. Lastly, the retrospective design of the study led to missing data on key variables, such as socio-economic and psychosocial factors, which could impact the results.

Conclusion

This study revealed an overall ART initiation rate of 152 per 1,000 person-days, with an estimated initiation proportion of 81%. The median time to ART initiation was relatively brief. Key predictors of early ART initiation included being women, disclosing HIV sero-status, having no baseline opportunistic infections (OIs), lacking HIV/TB co-infection, being tested through the VCT approach, and having children in the household. Providing comprehensive services, along with involving men counselors and creating male-friendly clinic environments, may help to address the root causes of delayed ART presentation among the general population and men specifically.

Acknowledgements

The authors like to acknowledge the study participants, data collectors, colleagues, and the Adama Hospital Medical College.

Author contributions

Conceptualization, YG, HL and EM; data curation, YG and HL; formal analysis, YG, HL, EM, and TGC; funding acquisition, YG; project administration, HL, EM, and TGC; supervision, HL, EM, and TGC; writing-original draft, YG, HL, EM, and TGC; writing-review & editing, YG, HL, EM, and TGC. All authors contributed to the article and approved the submitted version.

Funding

The author received no specific funding for this work.

Data availability

No datasets were generated or analysed during the current study.

Declarations

Competing interests

The authors declare no competing interests.

Received: 9 September 2024 / Accepted: 12 January 2025 Published online: 11 March 2025

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