

Time to Antiretroviral Therapy Initiation and Its Predictors Among Newly Diagnosed HIV-Positive People in Nekemte Town, Western Ethiopia: Claim of Universal Test and Treat

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Background: HIV continuum of care demands early ART initiation for all HIV-infected individuals. Early ART initiation reduces onward HIV transmission facilitating rapid viral suppression. Despite this, delayed ART use is a challenge among newly diagnosed HIV-positive individuals, and there is limited evidence on time to ART initiation among this group in Ethiopia. Thus, this study aimed to assess time to ART initiation and its predictors among newly diagnosed HIV-positive individuals in Nekemte town, Western Ethiopia.

Methods: An institution-based retrospective follow-up study was conducted on 518 newly diagnosed HIV-positive people from September 5, 2016 to December 20, 2020 at Nekemte town, Western Ethiopia. Data were collected from ART intake forms, registration log books and patient charts. The collected data were entered into Epi Data version 3.1 and STATA version 14.0 was used for analysis. Survival probability was checked graphically by Kaplan–Meier curve and statistically by Log rank test. Both bivariable and multivariable Cox Proportional hazards regression models were conducted to identify the predictors of ART initiation. Hazard ratio with 95% CI and p-value of <0.05 was used to declare a statistical significance.

Results: By the end of the follow-up, 371 (71.6%) individuals had initiated ART with an overall incidence rate of 51.9 per 1000 [95% CI: 54.07–66.32] person days; median time to ART initiation was 4 [IQR: 1–9] days. Being female (AHR = 1.33, 95% CI: 1.06–1.67), urban dwellers (AHR = 2.02, 95% CI: 1.37–2.97), having baseline OIs (AHR = 1.62, 95% CI: 1.60–4.30); being tested via VCT (AHR = 1.33, 95% CI: 1.02–1.74); linked from OPD (AHR = 0.64, 95% CI: 0.47–0.85); disclosing HIV sero-status (AHR = 2.07, 95% CI: 1.17–3.68); and college and above education level (AHR = 1.43, 95% CI: 1.00–2.0) were identified as significant predictors of early initiation of ART.

Conclusion: The proportion and incidence of ART initiation was high; a short median time to ART initiation was revealed in this study. Strictly screening OIs, encouraging HIV sero-status disclosure and voluntary HIV testing are recommended to increase early ART initiation.

Keywords: ART initiation, time to ART initiation, newly diagnosed HIV positive, Ethiopia

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Introduction

Background

HIV/AIDS continues to be a public health threat. By the end of 2018, about 74.9 million people were infected and 32 million had died due to acquired immune

deficiency syndrome (AIDS) related illness globally.¹ As the United Nation program on AIDS (UNAIDS) reported, by 2019, 38 million people were living with HIV and among them 1.7 million were newly infected and thousands had died of the disease.² With limited accessibility of care and services, Sub-Saharan African (SSA) countries including Ethiopia share the highest global burden of HIV/AIDS.^{2,3}

The advancement of ART accessibility leads to people living with HIV (PLHIV) to live much longer; reduces the number of people dying of AIDS; changes HIV infection into a manageable chronic disease and reduces onward HIV transmission.⁴⁻⁶ Thus, to start ART use immediately after the HIV diagnosis confirmed is recommended for all HIV-infected individuals regardless of their CD4 cell count level and clinical stage as in the universal test and treat (UTT) strategy.^{4,7} Timely ART start among PLHIV contributes a pivotal role to handle the epidemic and it shifts the focus of care from survival to improving quality of life through adherence, retention in care and speed up of viral suppression.⁸ In UNAIDS' ambitious plan to see globally an HIV prevalence fewer than 200,000 and to end new HIV infection by 2030, timely ART start is a pillar strategy because it has both treatment and prevention purpose.^{2,8}

Ethiopia has incorporated the UTT strategy in its national policy since 2016 and the current ART guideline is adhered to and implemented accordingly.⁹ The country exhibits variation in burdens of HIV across geographic and population groups.^{9,10} The HIV continuum of care follows steps such as universal HIV test, immediate ART start, and rapid viral suppression in which the full benefit of the ART will be achieved.¹¹⁻¹³

Previous studies reported that the time from getting tested for HIV to start of ART use in newly diagnosed HIV clients varies from as short as one day to longer than 12 months.¹⁴⁻¹⁸

In Ethiopia, most studies are conducted on late presentation to HIV diagnosis.^{10,19-25} There is limited information on how long it takes to start ART for newly diagnosed HIV-positive individuals and its predictors even though the information is essential in the era of UTT to strengthen the HIV continuum of care. The HIV continuum of care demands an immediate ART start and rapid viral suppression. However, a delay in starting ART is a great challenge among newly diagnosed HIV-positive individuals which may cost them with early mortality, high health-care costs and poor retention in care, low ART uptake and poor viral suppression, which is not only affect the health of

individuals but also has impacts for households, communities, and nationwide through affecting development and economic growth.²⁶⁻²⁹ Thus, this study aimed to assess time to ART initiation and its predictors among newly diagnosed HIV-positive people at Nekemte town, Western Ethiopia.

Methodology

Study Setting and Period

This facility based retrospective follow-up study was conducted in Nekemte town, Western Ethiopia among newly diagnosed HIV-positive individuals from September 5, 2016 to December 20, 2020. Nekemte town is a capital city of East Wollega Zone which is 321 km away from Addis Ababa in west direction. There are four governmental health facilities found in the town; two hospitals: Nekemte Specialized hospital (NSH) and Wollega University Referral hospital (WURH) and two health centers: Cheleleki health center and Bake Jama health center. In all these health facilities comprehensive HIV care services such as conducting HIV test, counseling, initiating ART and prevention of mother to child transmission (PMTCT) program are available according to the UTT strategy. The 520 study participants were proportionally allocated to the four health facilities based on number of HIV-positive people found in each facility. All newly diagnosed HIV-positive individuals who were tested for HIV since UTT at selected health facilities were included in the study whereas individuals with incomplete data were excluded from the study. Therefore, 384 study participants from NSH, 46 from WURH, 21 from Cheleleki Health Center and 69 from Bake Jama Health Center were selected and recruited to the study according to the newly diagnosed HIV-positive patients that were found at each health facility.

Eligibility Criteria

Inclusion Criteria

All newly diagnosed HIV-positive individuals at selected health facilities, aged 15 years old and above, and who were tested for HIV from September 5, 2016 to December 20, 2020 were included in the study.

Exclusion Criteria

Individuals whose data were incomplete, such as with no record of date of HIV diagnosis and date of ART initiation, were excluded from the study.

Sample Size Estimation

To calculate sample size for survival data, log rank method which considers power and hazard ratio (HR) of the study was used. The Log rank method considers proportional hazard assumption and adjustment of withdrawal rate wherein the value of log rank is equal with q or rate of events at the end of the study.³⁰

To calculate probability of events and survival function at time $(S_1)t$ and $(S_2)t$, STATA version 14 was used. Log rank with the command of “stpower logrank 0.5, hratio () power (0.8) wdprob (0.1)”, i.e. Log rank 0.5, withdrawal probability 10% and HR of different variables were taken from a previous study conducted on predictors of ART initiation among treatment naive PLHIV in Myanmar in south-east Asia.³¹ Finally, for this study the largest sample size was selected, which was 520.

Sampling Procedure

Data were retrieved from medical registration logbooks, ART intake forms and HIV testing and counseling logbooks. Profiles of the newly diagnosed HIV-positive people in selected health facilities were systematically recruited using their medical registration number (MRN) as sampling frame and included into the study every eighth interval (k).

Study Variables

Dependent Variable

Time to ART initiation (time in days from confirmed positive HIV diagnosis (starting point) to ART initiation or start (end point)).

Independent Variables

Socio-demographic factors: Age in years, marital status (single, married, widowed, and divorced), occupation status (unemployed, house wife, gov't employed, and private work), educational level (write and read only, primary school, secondary school, and college and above), religion (Orthodox, Protestant, Muslim, and Catholic), residence (rural, urban).

Baseline clinical and laboratory factors: Baseline CD4 cell count, WHO clinical stage, baseline OIs (Yes/No), functional status (working, ambulatory, bedridden), baseline comorbidity (Yes/No), TB screening (Yes/No), TB/HIV co-infection (Yes/No).

Personal and family factors: Disclosure status (Yes/No), partner HIV status (Positive/Negative/Unknown).

Structural and Regimen related factors: HIV test approach (VCT/PICT), years diagnosed for HIV (2016/2017/2018/2019/200), use baseline CPT (Yes/No), and use baseline IPT (Yes/No), and place of HIV diagnosis (hospital/health center).

Operational Definition

ART initiation (Event): Commencing of lifelong therapy after positive HIV diagnosis has confirmed and the first time at which newly diagnosed HIV-positive person start to collect ART.

Censored: Newly diagnosed HIV-positive people, who either died, transferred out, lost from follow-up before initiating ART, and not yet started ART when study was ended.

Functional Status

Working: Able to perform usual work in or out of the house; Ambulatory: Able to perform activities of daily living; Bedridden: Not able to perform activities of daily living.³³

Data Collection Tools and Quality Control

The data were collected using a checklist which was developed from different literatures in line with HIV testing and counseling services (HTCS) logbooks and ART intake forms. The checklist contains socio-demographic data, baseline clinical data, baseline laboratory data, personal related data, family related data, and structure or regimen-related data.

To assure the quality of data, one day of intensive training was provided for data collectors and supervisors by the principal investigator on clarity of tools and data handling including confidentiality assurance. Pre-test of the tool was conducted on 5% of patient's records before the actual data collection started to check the clarity of terms in the questionnaire. Accordingly, possible modification was carried out. Eight data collectors (clinical nurse) and four supervisors (BSc Nurse) participated in data collection. Completeness and consistency of the collected data were checked by the principal investigator on a daily basis. To ensure confidentiality, data were collected anonymously and the collected data were kept in a locked cabinet to avoid its access by a third body.

Data Management and Analysis

Epi data version 3.1 was used for data entry and further analysis was performed using STATA version 14.0. Data

were cleaned, edited, re-categorized and categorized prior to the actual analysis. Descriptive survival analysis such as life table and Kaplan–Meier function curve were computed to estimate survival probability. A day was used as time scale to calculate time to ART initiation. Person-days of observation was calculated as “date of ART started (event or censored) subtract date of positive HIV diagnosis confirmed”. Probabilities of ART initiation at different time intervals and cumulative survival probabilities were checked by life table. Both bivariable and multivariable cox regression model analysis was performed to investigate potential predictors of ART initiation. In bivariable Cox regression model analysis, predictors which revealed association with outcome variables at the p-value of <0.25 were included into the final multivariable Cox regression model analysis. Multivariable Cox proportional hazard regression was fitted using stepwise backward elimination of variables. Lastly, the model was selected by using Akaike’s Information criteria (AIC) that showed the smaller the value of the statistic, as best the model fit. Hazard Ratios (HR) with 95% confidence intervals was computed and statistical significance was declared at 5% level (p value < 0.05). Cox proportional hazards regression model was used to determine factors associated with risk of ART initiation by controlling confounding factors. To assess model adequacy for proportional Hazard model, Proportional Hazard assumption was checked and goodness-of-fit or overall model adequacy of Proportional Hazard Model was assessed.

Ethical Considerations

Ethical clearance was obtained from Ethical Review Committee of Institute of Health Science Wollega University with Ref. 043/IHRSPD/13. Permission letters were obtained from the respective health facilities administrative bodies.

Results

From September 5, 2016 to December 20, 2020, about 3965 individuals were newly diagnosed and found to be HIV positive in Nekemte town. Out of a total of 520 proposed study participants, 518 were followed retrospectively for a median time of 13.46 days [IQR: 10.06–16.86]; two participants were excluded due to lack of recorded date of HIV test. Out of the total study participants/observations (518), 147 (28.4%) were censored.

Socio-Demographic Characteristics of Study Participants

The median age of newly diagnosed HIV positive people was 35 [IQR: 27–41] years. The majority of the study participants (164; 31.66%) were found in age category of ≥ 40 years old. More than half of the study participants were females (285; 55%); the majority (320; 61.80%) were married and 194 (38%) respondents had attended formal education to the level of primary school. Regarding occupational status and religion of the participants; 156 (30%) relied on private work and 239 (46.10%) were Protestant, respectively. The majority of the respondents were urban dwellers (447; 86.30%) (Table 1).

Baseline Clinical and Laboratory Characteristics of Study Participants

The median CD4 cell count level of respondents was 334.5 [IQR: 176–562]; the median baseline hemoglobin level was 14.4 [IQR: 13.2–16.2] and the median BMI was 20.4 [IQR: 18.2–23.1]. The majority of respondents had CD4 cell count <500 cells/mm³ (337; 65.10%) and had an undetectable viral load (360; 69.5%); and the majority of respondents (404; 78%) had hemoglobin ≥ 11 mg/dl. Three-quarter s (394; 76%) of respondents had stage I of WHO clinical category, and almost all (469; 90.50%) presented with working functional status. Almost all respondents had no comorbidities (510; 98.5%); were screened for TB (495; 95.7%); and had no TB/HIV co-infection (476; 91.9%). Most respondents had no OIs (477; 92%), and the majority (313; 60.4%) had normal BMI (Table 2).

Facility and Structure Related Characteristics of Study Participants

The majority (369; 71.2%) of the respondents were tested for HIV via VCT approach; were linked to the ART clinic from OPD170 (32.8%); were tested for HIV in 2018 (143; 27.6%) and most of the HIV tests were performed at hospital (455; 87.8%); the majority had used baseline CPT prophylaxis (316; 61%) and baseline IPT prophylaxis (446; 86%), and most of the respondents (454; 87.6%) were from ART catchment area of selected health facilities (Table 3).

Personal and Family Related Characteristics of Study Participants

Almost all of the study participants (498; 96.1%) had disclosed their HIV sero-status and in more than half

Table 1 Socio-Demographic Characteristics of Newly Diagnosed HIV-Positive People in Nekemte Town, Western Ethiopia, 2016–2020

Variable Type	Categories	Frequency	Percentage (%)
Age	15–19 years old	20	3.9
	20–24 years old	58	11.2
	25–29 years old	96	18.5
	30–34 years old	81	15.6
	35–39 years old	99	19.1
	≥40 years old	164	31.7
Sex	Male	233	45.0
	Female	285	55.0
Marital Status	Single	100	19.3
	Married	320	61.8
	Divorced	68	13.1
	Widowed	30	5.8
Educational Status	Write and read only	113	21.8
	Primary school	194	37.5
	Secondary school	135	26.0
	College and above	76	14.7
Occupational Status	Unemployed	49	9.5
	House wife	154	29.7
	Gov't employed	149	28.8
	Private work	156	30.0
	Others*	10	2.0
Religion	Protestant	239	46.1
	Orthodox	223	43.1
	Muslim	47	9.1
	Catholic	9	1.7
Residence	Urban	447	86.3
	Rural	71	13.7

Note: *Drivers, car servants.

(277; 55.3%) the disclosure was to spouse. The majority of the respondents (463; 89.4%) reported having a regular sexual partner, and about half those partners had positive HIV sero-status (232; 50.2%). The majority (328; 63.3%) of respondents reported presence of children with age less than 15 years in their home and the majority (249; 76.2%) of those children's HIV sero-status was negative (Table 4).

Survival Status of Newly Diagnosed HIV Positive People

A total of 518 newly diagnosed HIV-positive people were followed for a mean time of 13.79 days [95% CI: 10.40–17.19] with total time at risk of 7147 person-days. The minimum and maximum follow-up time observed was 1 day and 366 days, respectively. Overall, nearly three-quarters (371; 71.6%) [95% CI: 67.4–75.2] of newly

diagnosed HIV positive people had initiated ART throughout the follow-up; 96 (18.5%) [95% CI: 15.4–22.1] were transferred out to other health facilities before ART initiation; 45 (8.7%) [95% CI: 6.7–11.7] individuals were lost to follow-up before starting ART and 6 (1.2%) [95% CI: 0.5–2.6] individuals died before they initiated ART (Figure 1).

ARTI_ Antiretroviral Initiation

To observe the estimate of the survival time, Kaplan–Meier and Nelson–Aalen Cumulative hazard estimation techniques were used. The graph of Nelson–Aalen Cumulative hazard estimations showed that an increase in the hazard rate has direct relation with the increment of time (Figure 2). The overall graph of Kaplan–Meier survivor function depicts that decrement of events over a follow-up period (Figure 3).

Table 2 Baseline Clinical and Hematologic Related Characteristics of Newly Diagnosed HIV-Positive People in Nekemte Town, Western Ethiopia, 2016–2020

Variable Type	Categories	Frequency	Percentage (%)
Baseline CD4 cell count	≥500 cell/mm ³	181	34.9
	<500 cell/ mm ³	337	65.1
Baseline viral load	TND	360	69.5
	<1000 copies/mL	112	21.6
	≥1000 copies/mL	46	8.9
Baseline Hemoglobin	≥11 mg/dl	404	78.0
	<11 mg/dl	114	22.0
Baseline WHO clinical stage	Stage I	394	76.0
	Stage II	72	14.0
	Stage III/ IV	52	10.0
Functional status	Working	469	90.5
	Ambulatory	32	6.2
	Bedridden	17	3.3
Comorbidities	Yes	8	1.5
	No	510	98.5
Baseline OIs	Yes	41	8.0
	No	477	92.0
Screened for TB	Yes	495	95.7
	No	23	4.4
HIV/TB co-infection	Yes	42	8.1
	No	476	91.9
BMI	≥25 kg/m ²	90	17.4
	18–24.99 kg/m ²	313	60.4
	≤17.99 kg/m ²	115	22.2

Abbreviations: HIV/TB, human immune virus and tuberculosis co-infection; BMI, body mass index; OIs, opportunistic infections; WHO, World Health Organization; TND, target not detected; CD4, cluster of differentiation molecular 4.

Incidence and Time to ART Initiation

The magnitude of initiated ART among newly diagnosed HIV-positive individuals by the end of follow-up was (371; 71.6%) [95% CI: 67.4–75.2] and the majority (264; 71.2%) of the ART initiation occurred within 7 days of a confirmed positive HIV diagnosis. An overall incidence rate of ART initiation was 51.9 per 1000 [95% CI: 54.07–66.32] person-days, and the median time to ART initiation (from confirmed positive HIV diagnosis to ART initiation) for newly diagnosed HIV-positive individuals was 4 [IQR: 1–9] days. The highest incidence rate of the ART initiation was observed within 7 days of enrollment to care which was 544.3/1000 person-days.

Predictors of ART Initiation Among Newly Diagnosed HIV-Positive People in Nekemte Town, Western Ethiopia, 2016–2020

To identify predictors of ART initiation, bivariable Cox regression analysis was done and each independent variable was analyzed with outcome variable, and the impact of individual variable on time to ART initiation was checked before model selection. All potential predictors that had p-value of ≤ 0.25 in bivariable Cox regression analysis were considered for multivariable Cox regression model analysis. Accordingly, 14 variables were selected to be included into multivariable Cox proportional hazard analysis. Then multivariable Cox proportional hazard

Table 3 Facility and Structural Related Characteristics of Newly Diagnosed HIV-Positive People in Nekemte Town, Western Ethiopia, 2016–2020

Variable Type	Categories	Frequency	Percentage (%)
HIV test approach	VCT	369	71.2
	PICT	149	28.8
Linked from	OPD	170	32.8
	Ward	145	28.0
	TB clinic	72	14.0
	STI clinic	17	3.2
	Others (ANC, PNC, MCH)	114	22.0
Years of tested for HIV	2016	79	15.3
	2017	120	23.2
	2018	143	27.6
	2019	78	15.0
	2020	98	18.9
Site tested for HIV	Hospital	455	87.8
	Health center	25	4.8
	Others	38	7.4
Use baseline CPT	Yes	316	61.0
	No	202	39.0
Use baseline IPT	Yes	446	86.0
	No	72	14.0
Reside within catchment area	Yes	454	87.6
	No	64	12.4

Abbreviations: TB, Tuberculosis; CPT, Cotrimoxazole Preventive Therapy; IPT, Isoniazid Preventive Therapy; HIV, Human immunodeficiency Virus; OPD, outpatient department; STI, sexually transmitted infections; ANC, antenatal care; PNC, postnatal care; MCH, mother and child health.

analysis was performed by using backward stepwise selection, and in the multivariable Cox proportional regression analysis model seven variables (sex, residence, presence of OIs, HIV test approach, linked site, HIV disclosure status and educational level) remained significantly associated with ART initiation.

Regarding the incidence rate of ART initiation among statistically significant variables, the incidence rate of ART initiation was 115.5/1000 PD among females vs 30.8/1000 PD among males, 104.3/1000 PD among urban vs and 12.7/1000 PD among rural, 70.1/1000 PD among disclosed sero-status vs 8.5/1000 PD among not disclosed HIV sero-status, 109.1/1000 PD among VCT vs 23.4/1000 PD among PICT and 87.8/1000 PD among no OIs vs 9.2/1000 PD among with OIs. The difference in ART initiation rate among covariates highlights the existence of a short time from HIV test to ART initiation for covariates with high incidence rate.

Accordingly, being female, urban residence, having baseline OIs, getting tested for HIV via VCT approach,

disclosing HIV sero-status and attending formal education to college and above level and linked to the ART clinic from OPD, ward, and TB clinic were independent predictors of ART initiation. Female respondents had 1.33 times higher hazard to initiate ART early compared with males (AHR = 1.33, 95% CI: 1.06–1.67). Individuals who came from urban areas were 2.02 times higher in initiating ART as early as possible when compared with rural dwellers (AHR = 2.02, 95% CI: 1.37–2.97). The hazard of initiation of ART early was 2.62 times higher in individuals with no baseline OIs when compared with their counterparts (AHR = 1.62, 95% CI: 1.60–4.30). Getting tested for HIV via VCT approach favors early ART initiation 1.33 times higher than that of PICT approach (AHR = 1.33, 95% CI: 1.02–1.74). Individuals who linked to ART clinic from OPD had 36% reduction in hazard of initiating ART early (AHR = 0.64, 95% CI: 0.47–0.85). Those who disclosed their HIV sero-status were 2.07 times more likely to initiate ART earlier when compared

Table 4 Personal and Family Related Characteristics of Newly Diagnosed HIV-Positive People in Nekemte Town, Western Ethiopia, 2016–2020

Variable Type	Categories	Frequency	Percentage (%)
HIV disclosure status	Disclosed	498	96.1
	Not disclosed	20	3.9
To whom disclosed	Spouse	277	55.3
	Own child	15	3.0
	Parents	179	35.7
	Siblings	8	1.6
	Relatives/friends	14	2.8
	Others*	8	1.6
Having partner	Yes	463	89.4
	No	55	10.6
Partner's HIV status	Positive	232	50.2
	Negative	216	46.8
	Unknown	15	3.0
Presence of <15 age children in family	Yes	328	63.3
	No	190	36.7
HIV status of the <15 age children	Positive	53	16.2
	Negative	249	76.2
	Unknown	25	7.6

Note: *Co-workers, nearby leader.

Abbreviation: HIV, human immunodeficiency virus.

with those individuals who did not disclose their sero-status (AHR = 2.07, 95% CI: 1.17–3.68); and respondents who attended educational level to college and above were 1.43 times more likely to initiate ART early when compared with individuals who could only write and read (AHR = 1.43, 95% CI: 1.00–2.03) (Table 5).

Discussion

Rapid ART initiation is one of the strategies to increase ART uptake, engagement in care and accelerate the viral suppression. In addition, rapid ART start can potentially reduce the time during which people with newly diagnosed HIV can transmit HIV through which the epidemic will be controlled as is the UTT goal. This study was conducted to

Survival Status

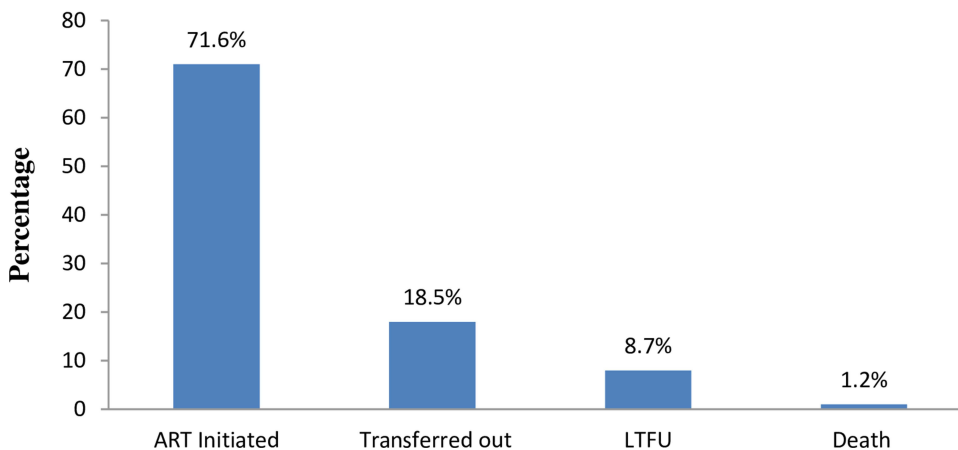


Figure 1 Test outcome of newly diagnosed HIV positive people in Nekemte town 2016–2020.

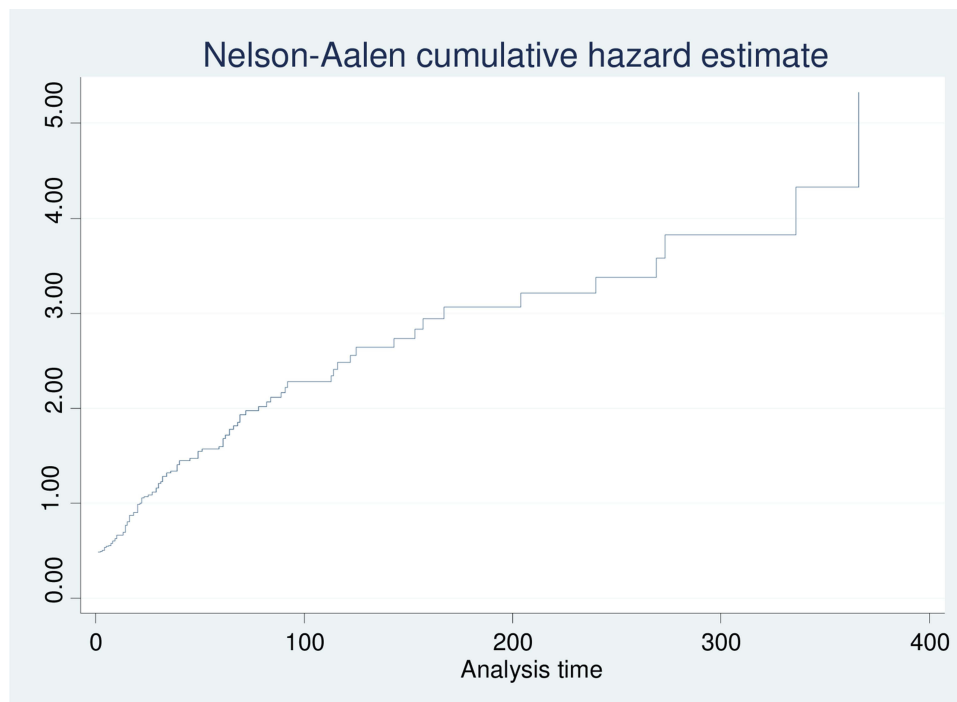


Figure 2 The Nelson-Aalen Cumulative Hazard of newly diagnosed HIV-positive people in Nekemte town from 2016–2020.

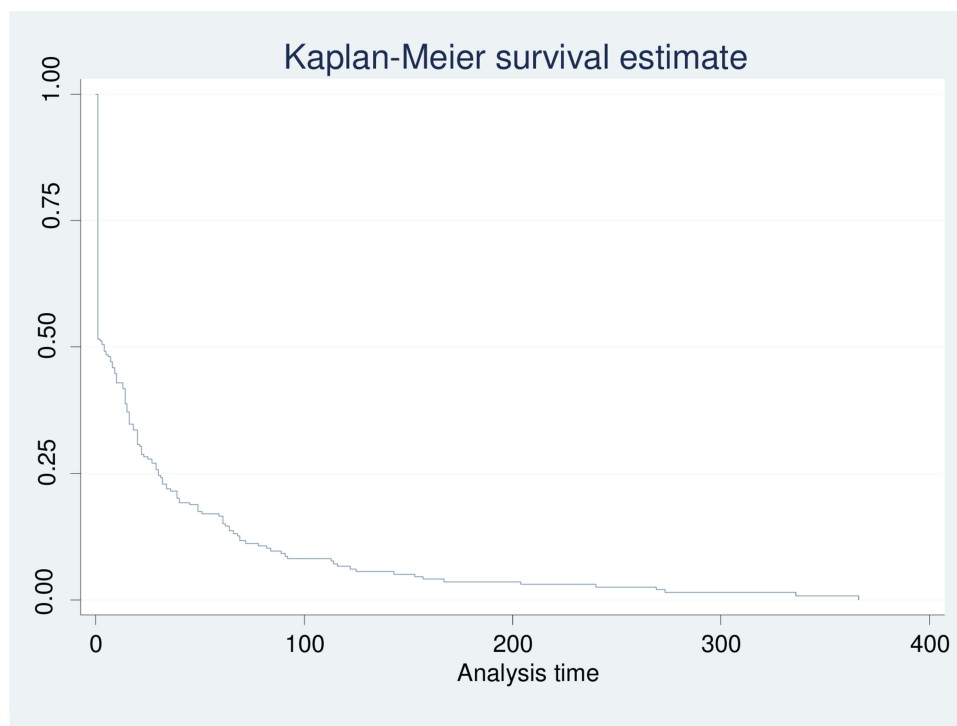


Figure 3 The overall Kaplan-Meier Survival function estimate of newly diagnosed HIV-positive people in Nekemte town from 2016–2020.

assess time to ART initiation, incidence and predictors of ART initiation among newly diagnosed HIV-positive people. Thus, the 518 study participants were recruited and

followed retrospectively to assess the time to ART initiation, incidence rate of ART initiation and its predictors. At the end of follow-up, overall 71.6% of them had initiated

Table 5 Bivariable and Multivariable Cox Proportional Hazard Model of Incidence and Predictors of ART Initiation Among Newly Diagnosed HIV-Positive People in Nekemte Town, Western Ethiopia, 2016–2020

Variables	Category	Survival Status		CHR/CI	AHR/CI	P-value
		Event	Censored			
Sex	Male	166	67	1 1.52(1.23–1.89)	1 1.33(1.06–1.67)	0.013
	Female	205	80			
Residence	Urban	319	128	3.05(2.14–4.36) 1	2.02(1.37–2.97) 1	0.001
	Rural	52	19			
WHO Clinical stage	Stage I	289	105	1 0.7(0.51–0.97) 0.93(0.64–1.35) 0.7(0.26–1.9)	1 0.84(0.60–1.16) 1.22(0.82–1.82) 0.84(0.29–2.43)	0.302 0.311 0.762
	Stage II	47	25			
	Stage III	31	12			
	Stage IV	4	5			
Presence of Comorbidity	Yes	8	0	1 3.49(1.53–7.95)	1 1.5(0.62–3.67)	0.364
	No	363	147			
Presence of OIs	Yes	30	11	1 3.79(2.41–5.94)	1 2.62(1.60–4.30)	0.001
	No	341	136			
TB/HIV Co-infection	Yes	36	6	1 2.13(1.44–3.14)	1 0.85(0.55–1.33)	0.495
	No	335	141			
HIV test approach	VCT	259	110	1.7(1.33–2.18) 1	1.33(1.02–1.74) 1	0.032
	PITC	112	37			
Linked from	OPD	115	55	0.71(0.53–0.94) 0.79(0.59–1.05) 0.73(0.52–1.03) 0.67(0.36–1.26) 1	0.64(0.47–0.85) 0.72(0.53–0.97) 0.69(0.48–0.99) 0.58(0.30–1.11) 1	0.003 0.035 0.049 0.103
	Ward	101	44			
	TB clinic	53	19			
	STI clinic	11	6			
	Others*	91	23			
Used IPT	Yes	341	105	1.51(1.03–2.21) 1	1.27(0.85–1.91) 1	0.235
	No	30	42			
Reside within catchment area	Yes	334	120	1.33(0.94–1.89) 1	0.97(0.66–1.44) 1	0.906
	No	37	27			
HIV Disclosure status	Disclosed	353	145	3(1.79–5.04) 1	2.07(1.17–3.68) 1	0.012
	No Disclosed	18	2			
Having regular partner	Yes	342	121	1.54(1.03–2.28) 1	1.19(0.78–1.82) 1	0.395
	No	29	26			
Presence of <15 years old children in home	Yes	246	82	1.49(1.19–1.87) 1	1.09(0.86–1.820) 1	0.464
	No	125	65			
Educational level	Write and read only	70	43	1 1.03(0.77–1.38) 1.25(0.89–1.64) 1.52(1.08–2.14)	1 1.04(0.77–1.41) 1.25(0.91–1.71) 1.43(1.00–2.03)	0.755 0.159 0.046
	Primary school	129	65			
	Secondary school	109	26			
	College and above	63	13			

Note: *ANC, PNC, MCH.

Abbreviations: TB, Tuberculosis; CPT, Cotrimoxazole Preventive Therapy; IPT, Isoniazid Preventive Therapy; HIV, Human immunodeficiency Virus; OIs, Opportunistic Infections; WHO, World Health Organization; CHR, Crude Hazard Ratio; AHR, Adjusted Hazard Ratio; CI, Confidence Interval.

ART. Being female, urban dwellers, disclosing HIV sero-status, college and above educational level, having no baseline OIs, linked from OPD and getting tested for HIV via VCT approach were the predictors of early ART

initiation. The overall incidence rate of ART initiation that was revealed in this study was 51.9/1000 person-days observation in which 67.4% [95% CI: 59.3–73.5] of them initiated the ART on the same day of confirmed

positive HIV diagnosis. This result is in line with a previous study result done in Taiwan which revealed rapid ART initiation of 68.3%.³⁴ However, this result is higher than a study result conducted in Ethiopia,³⁵ and South Africa,³⁶ which reported the rate of the same day ART initiation among newly diagnosed HIV positive people was 40.90% and 40.4%, respectively. This inconsistency might be attributable to the study period and setting difference. The current study was conducted in multiple institutions including hospitals and health centers whereas the previous studies were done in a single institution, this might reduce the magnitude of the same day ART initiators. Additionally, the previous studies were done when the treat-all program was launched for the first time which decreases the magnitude of the same ART initiators due to lack of trained health providers on the UTT strategy, and also the patients may be more likely to refuse to accept it due to inadequate knowledge on health benefits of immediate ART initiation. Initiating ART as early as possible will positively affect the health outcome of HIV-infected individuals in that many people will be retained in care, adhere to lifelong therapy, attrition rates will be reduced and durable viral suppression will be achieved and maintained within a short period.

In this particular study, the overall median time to ART initiation was 4 [IQR: 1–9] days. This figure implies that the UTT strategy of putting all HIV-infected individuals on ART regardless of their CD4 cell count and clinical stage is applying at the study setting in a fitting way. This result is in line with study results from Kampala, Uganda that reported the median time to ART initiation was 6 days,⁸ and review of evidence regarding rapid ART initiation, which revealed that newly diagnosed HIV-positive individuals on average started ART within 7 days of a confirmed positive HIV diagnosis.³⁷ However, this is shorter than in study results conducted in Myanmar,³² Croatia,³⁸ and Melbourne, Australia³⁹ which reported the median time to ART initiation as of 29, 30, and 77 days respectively. The variation may be due to the different criteria used to initiate ART for newly diagnosed HIV-positive individuals. In previous studies eligibility criteria of CD4 cell count and WHO clinical stage were used to put HIV-infected individuals on ART which could take a long time. Currently, the universal test and treat strategy is working which recommends early ART initiation even including on the same day of confirmed positive HIV diagnosis, which probably shortens the median time to start ART. This finding has an implication for the proper

implementation of HIV continuum of care to the study settings, which facilitates earlier viral suppression and reduces onward infection transmission.³⁹

This study also revealed that the hazard of initiating ART as early as possible was shorter in females, urban dwellers, and individuals with baseline OIs when compared with their counterparts of male, rural dwellers, and those without baseline OIs. This finding is supported by study findings from Myanmar, South Africa, and Ekurhuleni,^{32,40,41} the reason why females initiated ART earlier than men may be attributed to conditions such as being pregnant, lactating and in labor and delivery, during which they are tested for HIV, and the providers strictly advise them to initiate the therapy early to prevent mother to child HIV transmission. Thus, the women may accept the advice and try to minimize the probability of infecting her neonate through placenta, labor/delivery and breast feeding and are then enforced to take ART earlier. Urban dwellers initiated ART sooner than rural dwellers. This might be due to those who were residing in urban areas being nearby to health facilities, as well as having more awareness of the health benefits of early ART initiation than those who come from rural areas. Also, urban communities have different sources of information such as television, radio, internet and then accept the orientation and advice given from health providers. The individuals from rural areas are more affected by social stigma and negative attitudes pointed towards people infected with HIV and they refuse to start ART as early as possible. The possible reason that people without baseline OIs initiated ART earlier than those individuals with baseline OIs, is that when HIV and different OIs are diagnosed at the same time, the OIs need to be treated first and the patient needs to stay on OI treatment for a specified period of time to minimize immune reconstitution inflammatory syndrome (IRIS) and then ART can be followed. It is medically recommended to delay ART initiation to some extent to stabilize patients with OIs.

For individuals who were linked to ART chronic services from OPD, Ward and TB-clinic, longer time to ART initiation was revealed than among individuals who were linked from other health units such as ANC, MCH, and delivery ward. This finding is similar with a previous study conducted in Ethiopia which revealed that pregnant women were more likely to have initiated ART on the same day of confirmed positive HIV diagnosis.³⁵ Family planning, antenatal care and postnatal care are hospital units where the prevention of mother to child transmission

(PMTCT) of HIV program is applied the most so far, and that is why the initiation of ART as early as the same day of confirmed positive HIV diagnosis is strictly recommended with strong follow-up and convincing approaches.

Individuals who disclosed their HIV positive sero-status more initiated ART earlier than those who did not disclose it. This might be because disclosing one's own sero-status may enable the HIV-infected individual to get economic and social support from relatives; minimize HIV-related stigma which directly or indirectly encourages the patient to commence ART as early as possible and to adhere to the lifelong therapy and medical advice.^{42,43} Likewise, individuals who attended educational level up to the level of college and above initiated ART earlier than those who could write and read only. Education enables people to understand the positive outcome of lifelong therapy; increases the self-confidence to take decisions and change negative attitudes towards people living with HIV; educated people are more sociable, accept advice and direction that is provided by health providers as compared with those who are illiterate;^{44,45} another study result reported that among HIV-infected individuals who initiated ART, 82.8% were literate while the rest were illiterate.³² The possible explanation might be that those who are illiterate can be easily affected by HIV-related stigma; fear of being known to be HIV positive in their social circuit will outweigh the health benefits of early ART initiation and thus newly diagnosed HIV-positive illiterate individuals are put off taking ART early.

Regarding testing approaches, those who get tested for HIV through VCT initiated ART earlier than individuals who get tested via PITC approaches. This finding is supported by a previous study conducted in Ethiopia, which reported that people living with HIV who get tested through PITC were relatively delayed to initiate ART compared with those who get tested via VCT.⁴⁶ Having knowledge of the impact of a late diagnosis of HIV on future health outcome and perceiving self-behavioral risks to acquire the infection may encourage people to get tested and easily start ART as early as possible if found to be positive. Individuals who get tested through VCT were more knowledgeable on risky behaviors, health outcome of early ART initiation, and how to reduce onward transmission of the infection than those who were tested via provider initiation.

Limitation of the Study

Data were retrospective follow-up in which access to full information might be difficult due to unregistered outcomes.

The true incidence of ART initiation might be overestimated or underestimated because of incomplete documentation.

Conclusion

In this study, a higher proportion and incidence rate of ART initiation was revealed, and the median time to ART initiation was shorter when compared with studies previously done in Ethiopia and other Sub-Saharan Africa countries. Being female, urban dwellers, disclosing HIV sero-status, college and above educational level, having no baseline OIs, linked from OPD and getting tested for HIV via VCT approach were the predictors of early ART initiation. Given that, the UTT strategy needs to be applied and strengthened at the study setting.

Recommendation

Strictly screening OIs before ART initiation, encouraging further HIV sero-status disclosure and disseminating health information on benefits of volunteer HIV test should be strengthened and advocated to maintain universal test and treat strategy applicability. Researchers need to conduct further research to know whether the transferred-out clients were started on ART or not.

Abbreviations

HIV, human immunodeficiency virus; ART, antiretroviral therapy; CI, confidence interval; AHR, adjusted hazard ratio; OI, opportunistic infection; OPD, outpatient department; IQR, interquartile range; SSA, sub-Saharan Africa; AIDS, acquired immunodeficiency syndrome; UTT, universal test and treat; UNAIDS, United Nations program on AIDS; PLHIV, people living with HIV; NSH, Nekemte Specialized hospital; PMTCT, prevention of mother to child transmission; WURH, Wollega University referral hospital; HC, health center; MRN, medical registration number; WHO, World Health Organization; TB, tuberculosis; VCT, volunteer counsel and test; PITC, provider initiation test and counsel; IPT, isoniazid preventive therapy; CPT, cotrimoxazole preventive therapy, HTCS, HIV test and counsel services; AIC, Akaike's information criteria; TND, target not detected; PD, person-days.

Data Sharing Statement

All generated and analyzed data are included into this research article.

Ethical Approval and Consent to Participants

Ethical approval was obtained from Institutional Review Board of Institute Health Sciences, Wollega University. Formal permission letter was obtained from each health selected facility administrative body to get the records of study participants. The patient informed consent was not taken due to the retrospective nature of data in which all information was collected from the patients' medical records. The data were collected anonymously and maintained with confidentiality. All the procedure of the data collection was conducted according to the principles of Helsinki Declaration.

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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 articles; 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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