



Magnitude and Associated Factors of First-line Antiretroviral Treatment Failure among Adult HIV Patients at selected public Health in Addis Ababa, Ethiopia, 2023, Multi-center Cross-sectional Study

Mohammed Tessema^{1*}; Yohannes Godie²; Getachew Worku³; Getachew Woldeyohanes⁴; Wegayehu Zeneb Teklehaimanot¹; Leweyehu Alemaw Mengstie¹; Fikirte Kassaye⁵

¹Debre Berhan University, College of Health Science, Debre Berhan, Ethiopia.

²Debre Markos University, College of Health Science, Debre Markos, Ethiopia.

³Africa Medical College, Department of Health Science, Addis, Ababa, Ethiopia.

⁴Yekatit 12 Hospital Medical College, Department of Health Science, Addis, Ababa, Ethiopia.

⁵Dagmawi Mennelik Hospital Medical College, Department of Health Science, Addis, Ababa, Ethiopia.

*Corresponding Author(s): Mohammed Tessema

Debre Berhan University, College of Health Science,
Debre Berhan, Ethiopia.

Tel: +2510914360904; Email: mohat2213@gmail.com

Received: Oct 24, 2023

Accepted: Nov 22, 2023

Published Online: Nov 29, 2023

Journal: Annals of HIV/AIDS Research

Publisher: MedDocs Publishers LLC

Online edition: <http://meddocsonline.org/>

Copyright: © Tessema M (2023). *This Article is distributed under the terms of Creative Commons Attribution 4.0 International License*

Keywords: First line; HIV treatment failure; kirkos sub-city; Addis ababa.

Abbreviations: ART: Antiretroviral Therapy; CD4 cells: Cells with CD4 marker; DTG: Dolutegravir; EFV: Efavirenz; HIV: Human Immunodeficiency Virus; LTFU: Lost To Follow Up; NNRTI: Non-Nucleoside Reverse Transcriptase Inhibitor; NRTI: Nucleoside Reverse Transcriptase Inhibitor; NVP: Nevirapine; OI: Opportunistic Infection; PDR: Pretreatment drug resistance; PI: Protease Inhibitors, PLWHIV: People living with HIV; TDF: Tenofovir; 3TC: Lamivudine; ZDV: Zidovudine.

Abstract

Background: Failure of antiretroviral therapy means disease progression and a high risk of death after initiation of highly active antiretroviral therapy. Failure of first-line ART is becoming a growing problem. ART failure represents a major challenge in HIV/AIDS treatment in resource-limited settings, particularly in Ethiopia.

This study aimed to assess the magnitude and associated factors of first-line antiretroviral treatment failure among HIV-positive adult patients in high-burden health centre in the Kirkos sub-city of Addis-Ababa, Ethiopia.

Method: A retrospective cross-sectional study was conducted among 350 PLHIV patients charted who were followed up from May 12, 2022, to May 12, 2023, in selected public health centers. A simple random sampling technique was used to select the study participants. Data were collected through face-to-face interviews using a structured questionnaire and by reviewing medical records charts in HIV patients using a constructive checklist. Binary logistic regression analysis was used to identify the magnitude of treatment failure. Finally, a P-value < 0.05 in the final model was used to declare the level of significance.

Results: This study revealed that the magnitude of treatment failure among patients on first-line HIV treatment was 21.7%, CI (17.4-25.7). Being not disclosed (AOR: 2.97, CI: 1.35-6.57), presence of malnutrition (AOR: 2.7, CI: 1.11-

Cite this article: Tessema M, Godie Y, Worku G, Woldeyohanes G, Teklehaimanot WZ, et al. Magnitude and Associated Factors of First-line Antiretroviral Treatment Failure among Adult HIV Patients at selected public Health in Addis Ababa, Ethiopia, 2023, Multi-center Cross-sectional Study. ANN HIV/AIDS Res. 2023; 2(2): 1003.



6.60), TB as an opportunistic infection (AOR: 2.35, CI: 1.13-4.88), loss of follow-up (AOR: 4.07, CI: 1.86-8.87), and poor drug adherence (AOR: 3.55, CI: 1.35-9.32) were the factors associated with treatment failure.

Conclusion: The failure rate of antiretroviral treatment was relatively high in this study. Therefore, different interventions have been proposed to different stakeholders to address this critical issue at different levels by acting on the identified factors to minimize this alarming rate of treatment failure.

Introduction

Globally, it is estimated that 36.9 million people were living with HIV, in 2017. Sub-Saharan Africa remains significantly affected, accounting for 69.5% of the people living with HIV. Ethiopia is among the SSA countries most affected by HIV/AIDS, with an estimated 710,000 people living with HIV in 2016 [2,6].

Ethiopia is one of the low-income nations with a high burden of HIV/AIDS, which accounts for 70 disability adjusted life years per 100,000 people [1]. Access to highly active antiretroviral therapy in Ethiopia started in 2005, and reached 420,000 people from 716, 418 people living with HIV/AIDS by 2016 ART [2,3].

Findings from the study conducted in Sub-Saharan Africa (SSA) indicated first-line ART treatment failure is 16%(4). Evidence indicated that about 15.3% of people living with HIV/AIDS who were on first-line ART treatment-experienced first-line ART treatment failure [5]. In the northern part of Ethiopia ART treatment failure account 20.3%, 13.2%,and 14.7% with clinical, immunological, and virological failure respectively [6].

Treatment failure occurs when a combination of the ART regimen fails to control HIV infection. This could be virologic, immunologic, and/or clinical failure [6].

Treatment failure can be a virological, immunological, or clinical failure [7]. Even though ART decreases the rate of death from HIV/AIDS, treatment failure has become common. At this time, more attention is given to increasing the availability and accessibility of ART without considering the rising rate of its treatment failure [1]. In Sub-Saharan Africa, many patients who experience treatment failure do not switch to potent second-line regimens due to resource limitation, yet those who remain on failing first-line regimens experience disproportionately higher morbidity and mortality compared to those who switch [2].

Access to highly active antiretroviral therapy in Ethiopia started in 2005 and reached 420,000 people out of 716,418 people living with HIV/AIDS by 2016 [12,13]. Even though ART is not a curative medicine, access to ART has played a vital role in the clinical management of HIV-infected individuals by reestablishing immune function and preventing morbidity and mortality. ART is also expected to play a significant role in reducing new HIV infections by 2020 [7]. The adult HIV prevalence in Ethiopia is 0.9%, with 2.9% in urban and 0.4% in rural settings. The incidence of a new infection is also at a steady state, with below three-fourths of People Living with HIV enrolled in antiretroviral therapy in the country [6]. Developing treatment-adherence-centered interventions with a focus on patients who have low socio-economic status is needed to reduce treatment failure and a high rate of treatment failure indicates a low qual-

ity of care [9].

A recent study showed that above 95% adherence to the ART regimen is required for HIV-infected patients to reach full viral suppression, but sustaining its adherence level requires accurate and consistent monitoring activities, and this is a major challenge for sub-Saharan African countries like Ethiopia [8]. There are limited studies in our country, in particular, there is no study conducted in this area. Therefore, this study was conducted to assess the magnitude and Associated Factors of First-line Antiretroviral Treatment Failure among Adult HIV Patients at High Load Health Centers in Kirkos Sub- City, Addis Ababa, Ethiopia.

Methods

Study area, design, setting, and period

An institutional based retrospective cross-sectional study was conducted in Addis Ababa, the capital city of Ethiopia, has 11 subcities, of which Kirkos subcity is the one located at the center of the capital in Kirkos, a sub city of Addis Ababa, Ethiopia. According to the Ethiopian Population and Health Survey, 2017 this sub-city has 8 public health centers, a total population of 317,879 residents, and 8,094 ARTs. There are a total of 7 health centers in Kirkos subcity. The health centers have departments, including ART clinics, outpatient departments, emergency departments, laboratory, pharmacy, TB, ART clinic, MCH, under five-year service, biomedical service, health information handling and management, and administration and finance department. The ART clinic is one of the departments in the health center that provides services for HIV/AIDS patients. The study was conducted from May 12, 2022, to May 12, 2023.

Source and study population

All adult patients who were on first-line ART had at least a six-month follow-up and fulfilled the inclusion criteria at high-load public health centers in Addis Ababa's Kirkos sub-city within the study period.

Eligibility criteria

All adult patients on first-line antiretroviral treatment who were attending the ART services and willing to participate in the study during the data collection period were included. On the other, patients who had aged less than 18 years on ART, and recently started ART with took less than 6 months were excluded.

Sample size determination and procedure

The sample size was calculated by using a single population proportion formula with study conducted at Mettu Karl Referral Hospital, Ethiopia prevalence was 29.3% with a 95% confidence level, and a 5% margin of error was considered [6]. The calculated sample size was 318. After adding a 10% non-response rate, the final sample is 350. The sample for each health center was proportionally allocated based on the number of clients in their ART clinics who are currently on ART follow-up. Finally, simple random sampling techniques were used to select study subjects from all selected health centers.

Data collection instrument and procedure

The Data were collected through face-to-face interviews with adult HIV patients using a structured questionnaire and by reviewing patient charts of HIV patients who fulfilled the inclusion criteria. The data collection tools were adapted from different literature [6,9,10]. It had four parts; a questionnaire consisting

of socio-demographic factors, clinical and behavioral factors, and antiretroviral treatment-related factors. Data were collected by five BSc nurses who had experience in data collection.

Data quality assurance

The questionnaire was first prepared in English and translated to Amharic, then back-translated to English by two language experts. One day of training was given to data collectors and supervisors. Moreover, a pretest was conducted on 5% of the final sample size at May chew Health Centre. Furthermore, continuous supervision and daily checking were conducted by the supervisor and principal investigator.

Data processing and analysis

The data were checked for completeness, cleaned, coded, and entered into Epi data version 4.6, then exported to SPSS version 25 for further analysis. Descriptive statistics were made. The Hosmer-lemeshow goodness-of-fit test was used to determine model fitness and the multi-collinearity test was used to detect the correlation between independent variables. That variable at bivariable analysis, a p value less than 0.25 was entered into multi-variable analysis. Finally, the adjusted odds ratio with their 95% CI was computed and a variable with a p-value less than 0.05 was considered as significantly associated with First-line ART treatment failure.

Operational definition

Adherence: the extent to which a patient continues the agreed-upon mode of treatment or intervention as prescribed.

Adults: In this study, participants aged 18–64 years are considered as adults.

Poor adherence: Less than 85% adherence, which is defined as missing greater than or equal to five doses out of 30 doses or greater than 10 doses from 60 doses [11,12].

Fair adherence: 85%-94% adherence, which is defined as missing two to four doses out of 30 doses or four to nine doses from 60 doses [12].

Good adherence: Greater than or equal to 95% adherence i.e. missing less than or equal to one out of 30 doses or missing less than or equal to two from the 60 prescribed doses [12].

ARV: Antiretroviral drugs used for the treatment of HIV infection.

Treatment failure: Clinical failure occurs when there is a new or recurrent WHO stage 3 or 4 condition.

Results

Socio-demographic characteristics of respondents

All the required 350 study participants were interviewed with a response rate of 100%. About 116 (33.1%) of the respondents were within the age group of 18-29 years. Of the total respondents, 164 (46.9%) were patients living alone in the house (Table 1).

Table 1: Socio-demographic characteristics of First Line Antiretroviral Treatment Failure among Adult HIV patients public selected Health centers in, Addis Ababa, Ethiopia, 2023 (n=350).

Variables		Frequency	Percent
Sex	Male	110	31.4
	Female	240	68.6
Age (in years)	18-29	116	33.1
	30-39	109	31.1
	40-49	77	22.0
	>50	48	13.7
Marital status	Single	146	41.7
	Married	84	24.0
	Divorced	96	27.4
	Widowed	24	6.9
Educational status	Unable to read and write	76	21.7
	Grade 1-6	112	32.0
	Grade 8-12	96	27.4
	Diploma	41	11.7
	Degree and above	25	7.1
Residency	Urban	314	89.7
	Rural	36	10.3
Distance to ART clinic	<10 km	312	89.1
	>10 km	38	10.9
Patients living condition	Alone in the house	164	46.9
	Alone on the street	34	9.7
	With family /friends	124	35.4
	Others	28	8.0
Patients functional status	Working	262	74.9
	Bedridden	26	7.4
	Ambulatory	62	17.7

Table 2: Clinical and behavioral factors of First Line Antiretroviral Treatment Failure among Adult HIV patients public selected Health centers in, Addis Ababa, Ethiopia, 2023.

Variables (n=350)		Frequency	Percent
Illness	Working	262	74.9
	Bedridden	26	7.4
	Ambulatory	62	17.7
	Yes	87	24.9
Body mass index	<16 kg/m ²	39	11.1
	16.01-18.5 kg/m ²	293	83.7
	> 18.5 kg/m ²	18	5.1

Opportunity infection after initiation of ART	Yes	275	78.6
Presence of malnutrition during ART initiation	Yes	39	11.1
Patients TB co Infection initiation on ART	Yes	56	16.0
Patient taken co-trimoxazole	Yes	116	33.1
Baseline CD4 results	<100 cells/mm ³	63	18.0
	101-349 cells/mm ³	188	53.7
	>350 cells/mm ³	99	28.3
Current CD4 results	<100 cells/mm ³	12	3.4
	101-349 cells/mm ³	70	20.0
	>350 cells/mm ³	268	76.6
First viral load at six months after initiation of ART	<1000 copies	327	93.4
	UH>1000 copies	23	6.6
Current viral load or second viral load	<1000 copies	338	96.6
	>1000 copies	12	3.4
History of alcohol intake	Yes	75	21.4

Clinical and behavioral factors of the patient

Most of the 263 (75.1%) patients were not disclosed. Most 268 (76.6%) of respondents were HIV/AIDS clinical WHO stage was Stage I. In this study 275 (78.6%) patients had opportunistic infections. Of the total participants, 56(16.0%) of patients had TB co-infection (Table 2).

In this study more than fifty percent of respondents 268(76.6%) were WHO stage 1 patient (Figure 1).

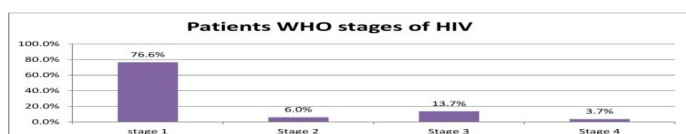


Figure 1: Patients WHO stages of HIV treatment failure from selected public health centers in Addis Ababa, Ethiopia, 2023.

Antiretroviral treatment factors of patient

About 312 (89.1%) of patients' adherence status were good, and 302 (86.3%) were keeping appointment schedule through came on time (Table 3).

Among the total respondents, 76 (21.7%) of Adults HIV patients were First line antiretroviral treatment failure (Figure 2).

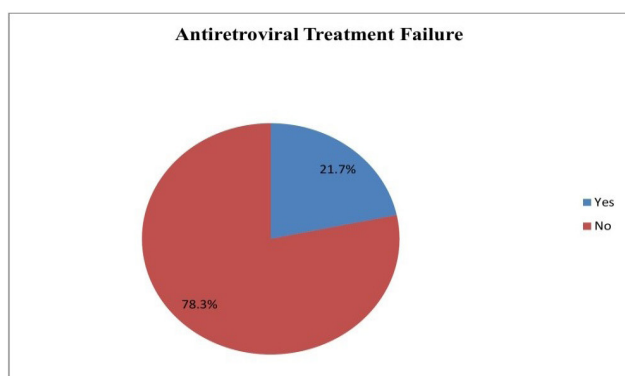


Figure 2: First line antiretroviral treatment failure among Adult HIV patients at selected public health center in Addis Ababa, Ethiopia, 2023.

Table 3: Antiretroviral Treatment-related factors of First Line Antiretroviral Treatment Failure among Adult HIV patients selected public health centers, Addis Ababa, Ethiopia, 2023.

Variables (n=350)		Frequency	Percent
Patients' initial ART regimen	TDF/3TC/DTG	200	57.1
	ZDV/3TC/DTG	15	4.3
	TDF/3TC/EFV	116	33.1
	ZDV/3TC/EFV	19	5.4
Duration of ART on months	6–24 months	218	62.3
	25-48 months	65	18.6
	49-72 months	50	14.3
	>73 months	17	4.9
First-line art drug substitution	None	343	98.0
	Once	7	2.0
Type of treatment failure (n=76)	Clinical	54	15.4
	Immunological	10	2.9
	Virological	12	3.4
Adherence status of patients	Good	312	89.1
	Fair	18	5.1
	Poor	20	5.7
Patients appointment schedule	Came on time	302	86.3
	Came late	38	10.9
	Came early	10	2.9
Patient history of loss to follow up	Yes	44	12.6
Patients drug adherence	≥95%	293	83.7
	<95%	57	16.3
Patients drug interruption	Yes	83	23.7

Table 4: Bi-variable and multivariable analysis of associated factors of First Line ART Failure among Adult HIV patients in selected public Health centers, Addis Ababa, Ethiopia, 2023.

Variables (n=350)	Category	Treatment failure		COR (95% CI)	AOR (95% CI)	P-value
		No	Yes			
Age	18-29	85 (73.3%)	31 (26.7%)	0.98 (0.46-2.09)	0.97 (0.40-2.31)	0.939
	30-39	98 (89.9%)	11 (10.1%)	0.30 (0.12-0.74)	0.36 (0.12-1.03)	0.057
	40-49	56 (72.7%)	21 (27.3%)	1.01 (0.45-2.27)	1.31 (0.50-3.41)	0.580
	>50	35 (72.9%)	13 (27.1%)	1	1	
Disclosure status	No	199 (75.7%)	64 (24.3%)	2.01 (1.03-3.92)	2.97 (1.35-6.57)	0.007*
	Yes	75 (86.2%)	12 (13.8%)	1	1	
Opportunistic infection	Yes	208 (75.6%)	67 (24.4%)	2.36 (1.12-4.99)	2.11 (0.88-5.03)	0.093
	No	66 (88.0%)	9 (12.0%)	1	1	
Presence malnutrition	Yes	22 (56.4%)	17 (43.6%)	3.30 (1.65-6.60)	2.71 (1.11-6.60)	0.028*
	No	252 (81.0%)	59 (19.0%)	1	1	
TB co-infection	Yes	37 (66.1%)	19 (33.9%)	2.14 (1.14-3.98)	2.35 (1.13-4.88)	0.023*
	No	237 (80.6%)	57 (19.4%)	1	1	
Baseline CD4 result	<100 cells/ mm ³	53 (84.1%)	10 (15.9%)	0.53 (0.24-1.19)	0.43 (0.17-1.09)	0.075
	101-350 cells/ mm ³	148 (78.7%)	40 (21.3%)	0.76 (0.43-1.34)	0.85 (0.41-1.76)	0.664
	> 350 cells/ mm ³	73 (73.7%)	26 (26.3%)	1	1	
History of alcohol	Yes	54 (72.0%)	21 (28.0%)	0.64 (0.36-1.15)	1.80 (0.92-3.53)	0.087
	No	220 (80.0%)	55 (20.0%)	1	1	
lost to follow-up	Yes	23 (52.3%)	21 (47.7%)	4.17 (2.15-8.06)	4.07 (1.86-8.87)	0.000*
	No	251 (82.0%)	55 (18.0%)	1	1	
Drug adherence	≥95%	226 (77.1%)	67 (22.9%)	2.48 (1.02-6.03)	3.55 (1.35-9.32)	0.010*
	<95%	48 (84.2%)	9 (15.8%)	1	1	

*=Statistically significant at p-value <0.05 with 95% CI.

Factors affecting first-line ART failure

Binary logistic regression analysis was used to identify the magnitude of treatment failure. In this study, being not disclosed was found to be one of the significant factors that increased the risk of first-line HIV treatment failure by 2.9 times (CI: 1.35–6.57) compared to disclosed patients. The presence of patients with malnutrition was 2.7 times (CI: 1.11-6.60) more likely to have treatment failure compared to their counterparts. This study found that developing TB as an opportunistic infection increases the risk of first-line HIV treatment failure by 2.3 fold (CI: 1.13–4.88). According to the findings of this study, loss to follow-up is the risk factor for first-line HIV treatment failure, which increases the odds by 4.1 times (CI: 1.86–8.87). Based on the findings of this study, poor drug adherence is another factor associated with first-line HIV treatment failure, which increases the risk by 3.55 folds (CI: 1.35–9.32) (Table 4).

Discussion

In this study, treatment failure of antiretroviral among adult HIV patients at high-load public health centers was 21.7% with a 95% CI of 17.4–25.7. This was in line with the patient's treatment failure reported in Sub-Saharan Africa [13]. This might be because the contributing factors for first-line HIV treatment failures in developing countries, including Ethiopia, are almost identical. This means most Sub-Saharan African countries suffer from malnutrition, co-infection, poor adherence, and poor disclosure habits due to different cultural and behavioral factors [8,10,14].

However, the findings of this study were higher than those of the systematic review conducted in Ethiopia [7]. This significant difference might be due to the difference in study quality. This means that a systematic review is the review of the literature that took the pooled prevalence resulting from high to low considerations.

The magnitude of this study is found to be less than the study conducted in South West Shoa [1]. The possible explanation for this difference might be due to the difference in socio-demographic, cultural, and adherence-related issues. This means the present study was conducted in Addis Ababa, where the HIV patients may be more educated and committed enough to the treatment compared with those found in rural areas of South West Shoa [15].

In this study, being not disclosed was found to be one of the significant factors that increased the risk of first-line HIV treatment failure by 2.9 times (CI: 1.35–6.57) compared to disclosed patients. This finding is similar to the study conducted in [7]. This might be due to the scientific fact that disclosure of HIV status improves adherence to antiretroviral therapy and increases the chance of virological suppression and retention in care [16]. Contrary to this, a lack of disclosure may cause fewer adherences, which end up with treatment failure.

Patients with malnutrition were 2.71 times (CI: 1.11-6.60) more likely to have treatment failure compared to their counterparts. This finding is similar to the result of a case-control

study conducted in Mettu Karl Specialized Hospital, southwest Ethiopia [9]. This might be due to the direct relationship between opportunistic infection and nutritional status, in which under nutrition significantly causes opportunistic infections, which leads to treatment failure. Malnutrition increases viral replication and accelerates the progression of HIV disease by decreasing CD4 T cells, suppressing delayed hypersensitivity, and altering T-cell responses. For this reason, malnutrition has a poor prognosis for clinical outcomes [17,18].

This study found that developing TB as an opportunistic infection increases the risk of first-line HIV treatment failure by 2.35-fold (CI: 1.13–4.88). This finding is supported by previous studies conducted at different times [9,14]. This might be due to the scientific fact that TB infection hurts the immune response to HIV, which accelerates the progression from HIV infection to AIDS and, in turn, leads to long-lasting immune suppression, which can increase viral load or cause treatment failure [19].

According to the findings of this study, loss to follow-up is the risk factor for first-line HIV treatment failure, which increases the odds by 4.07 times (CI: 1.86–8.87). This is similar to the conclusion of the case-control study conducted in Mettu Specialized Hospital in Ethiopia [9]. Patients who are lost to follow-up while on treatment compromise their health and the long-term success of antiretroviral therapy programs. ART significantly reduced mortality and improved the life expectancy of HIV-infected patients, but this attainment depends on regular patient follow-up. Lost to follow-up, would result in serious consequences, such as drug toxicity, treatment failure, and drug resistance [16].

Based on the findings of this study, poor drug adherence is another factor associated with first-line HIV treatment failure, which increases the risk by 3.55 folds (CI: 1.35–9.32). This finding is in line with previously conducted studies in different areas [9,14]. This could be explained by the fact that barriers to antiretroviral therapy adherence included side effects of the therapy and financial constraints limiting access to food, transport, and medication, cultural and religious factors, a lack of spouse support, stigma, and discrimination [20]. Adherence to therapies is a primary determinant of treatment success. Failure to adhere is a serious problem that affects not only the patient but also the health care system. Medication non-adherence in patients leads to substantial worsening of disease, death, and increased healthcare costs [21]. Therefore, poor adherence causes multi-factorial problems with the medication, which end up in failure.

Limitations of the study

A cross-sectional study design was used in this study. This type of study design shows the exposure and outcome at the same point in time, Cannot formulate a cause-and-effect relationship, and using secondary data like relying on past information which can be changed subsequently.

Conclusion

This study found that the magnitude of treatment failure was high as compared to different studies. Being not disclosed, presence of malnutrition TB as an opportunistic infection, loss of follow-up, and poor drug adherence were the factors associated with treatment. Therefore, special attention should be given to those individuals who have the above factors to minimize and prevent treatment failure.

Acknowledgment

First of all, I would like to acknowledge Africa Medical College for giving me this chance to do this thesis. I would also like to thank the College of Health Science Library, I am grateful for the assistance and guidance which were being. Finally, I would like to thank all study participants, data collectors, and supervisors who participated in this study.

Author's contribution

All authors were equally involved in the conception, study design, execution, acquisition of data analysis, and interpretation. As well as took part in drafting, and critically reviewing the article; wrote the manuscript paper, and prepared all the components of the manuscript and process for publication. All authors reviewed the final draft of the manuscript. Other ways I accept all components. Thanks and all the best.

Data sharing statement

The data used to support the findings of this study are available from the corresponding author upon request

Funding

No funding for publication

Declaration of conflicting interests

The authors declared no potential conflicts of interest with respect to the research or authorship.

Ethical consideration

Ethical approval was obtained from the Institutional Review Board (IRB) of the Africa Medical College School of Nursing and Midwifery department. Approval letter was obtained from the medical directors and relevant department heads at each healthcare facility.

Informed consent

Institutional approval was obtained by contacting the regional health department before conducting the study. Informed written consent was also obtained from the medical directors of the healthcare facility.

References

1. Misganaw A, Mariam DH, Araya T, Ayele K. Patterns of mortality in public and private hospitals of Addis Ababa, Ethiopia. *BMC public health*. 2012; 12: 1-9.
2. Alfvén T, Erkkola T, Ghys P, Padayachy J, Warner-Smith M, Rugg D, et al. Global AIDS reporting-2001 to 2015: Lessons for monitoring the sustainable development goals. *AIDS and Behavior*. 2017; 21: 5-14.
3. Bain LE, Nkoke C, Noubiap JJN. UNAIDS 90–90–90 targets to end the AIDS epidemic by 2020 are not realistic: comment on “Can the UNAIDS 90–90–90 target be achieved? A systematic analysis of national HIV treatment cascades”. *BMJ global health*. 2017; 2: e000227.
4. Ejigu S. First Line Antiretroviral Treatment Failure and Factors Associated with It in Addis Ababa, 2009: Addis Ababa University; 2009.
5. Endalamaw A, Mekonnen M, Geremew D, Yehualashet FA, Tesera H, Habtewold TD. HIV/AIDS treatment failure and associated factors in Ethiopia: Meta-analysis. *BMC Public Health*.

- 2020; 20: 1-12.
6. Bereda G, Bereda G. Prevalence of, and Factors Influencing First Line Antiretroviral Treatment Failure among Adult HIV Patients at Antiretroviral Treatment Clinic of Mettu Karl Referral Hospital, South Western, Ethiopia: A Prospective Cross-Sectional Study, 2021. *Int J Virol AIDS*. 2021; 8: 075.
 7. Assemie MA, Alene M, Ketema DB, Mulatu S. Treatment failure and associated factors among first line patients on highly active antiretroviral therapy in Ethiopia: A systematic review and meta-analysis. *Global health research and policy*. 2019; 4: 1-10.
 8. Endalamaw A, Mekonen M, Geremew D, Ambaw F, Tesera H, Habtewold TD, et al. Evidence that poor HAART adherence has a great impact on HIV/AIDS treatment failure more than severity of illness and opportunity of infection in Ethiopia: Systematic review and meta-analysis. *BioRxiv*. 2018:440743.
 9. Mamo A, Assefa T, Negash W, Takelign Y, Sahiledinigl B, Teferu Z, et al. Virological and immunological antiretroviral treatment failure and predictors among HIV positive adult and adolescent clients in southeast Ethiopia. *HIV/AIDS-Research and Palliative Care*. 2022; 73-85.
 10. Ndziessi G, Aloumba AJ, Essie DEM, Niama AC, Mbele FG, Diafouka M, et al. Factors Associated with Antiretroviral Treatments Failure among HIV-Positive Patients in Congo: A Retrospective Cohort Study. *World Journal of AIDS*. 2020; 10: 201-214.
 11. Farley SM, Wang C, Bray RM, Low AJ, Delgado S, Hoos D, et al. Progress towards the UNAIDS 90-90-90 targets among persons aged 50 and older living with HIV in 13 African countries. *Journal of the International AIDS Society*. 2022; 25: e26005.
 12. Poku NK. UN political declaration on HIV and AIDS: Where to begin? *The Lancet*. 2016; 388: 743-744.
 13. Ngandu NK, Lombard CJ, Mbira TE, Puren A, Waitt C, Prendergast AJ, et al. HIV viral load non-suppression and associated factors among pregnant and postpartum women in rural north-eastern South Africa: A cross-sectional survey. *BMJ open*. 2022; 12: e058347.
 14. Zenu S, Tesema T, Reshad M, Abebe E. Determinants of first-line antiretroviral treatment failure among adult patients on treatment in Mettu Karl Specialized Hospital, South West Ethiopia; a case control study. *PLoS One*. 2021; 16: e0258930.
 15. Mulisa D, Tolossa T, Bayisa L, Abera T, Wakuma B. First-line virologic-based ART treatment failure and associated factors among adult HIV Positives in Southwest Shoa, Central Ethiopia. *Journal of the International Association of Providers of AIDS Care (JIAPAC)*. 2022; 21: 23259582221111080.
 16. Izudi J, Okoboi S, Lwevola P, Kadengye D, Bajunirwe F, et al. Effect of disclosure of HIV status on patient representation and adherence to clinic visits in eastern Uganda: A propensity-score matched analysis. *Plos one*. 2021; 16: e0258745.
 17. Molla M, Kebede F, Kebede T, Haile A. Effects of undernutrition and predictors on the survival status of HIV-positive children after started Antiretroviral Therapy (ART) in Northwest Ethiopia. *International Journal of Pediatrics*. 2022; 2022.
 18. Alebel A, Demant D, Petrucka P, Sibbritt D. Effects of undernutrition on opportunistic infections among adults living with HIV on ART in Northwest Ethiopia: Using inverse-probability weighting. *Plos one*. 2022; 17: e0264843.
 19. Faye LM, Hosu MC, Iruedo J, Vasaikar S, Nokoyo KA, Tsuru U, et al. Treatment Outcomes and Associated Factors among Tuberculosis Patients from Selected Rural Eastern Cape Hospitals: An Ambidirectional Study. *Tropical Medicine and Infectious Disease*. 2023; 8: 315.
 20. Kalungwe M, Mbalinda SN, Karonga T, Simwanza NR, Mumba Mtambo CM, et al. Exploring barriers to antiretroviral therapy adherence among pregnant women: A scoping literature review. *International Journal of Gynecology & Obstetrics*. 2022;159: 343-350.
 21. Jimmy B, Jose J. Patient medication adherence: Measures in daily practice. *Oman medical journal*. 2011; 26: 155.