



First-line virologic-based ART treatment failure and associated factors among adult HIV Positives in Southwest Shoa, Central Ethiopia

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Abstract

Background: The function of antiretroviral therapy is to enhance immunity and prevent the occurrence of opportunistic infection. But antiretroviral therapy showed a failure to manage infection after a time. Nowadays, an accepted criterion to confirm Antiretroviral therapy (ART) treatment failure is a virologic failure. Regarding this virologic failure, there are no well-addressed findings, especially in this study area. Therefore in this research, the magnitude and factors that contribute for virological ART treatment failure have been identified. **Methods:** Facilitybased cross-sectional study was conducted on adult patients taking ART. Data entry was conducted using Epi Data Version3 and exported to Stata SE version 14 for analysis. Bivariable logistic regression was used to find covariates significantly associated with first line ART treatment failure. In this case, variables with P -value $\leq .25$ were a candidate for multiple logistic regressions. A backward logistic regression model was used. Finally, variables with P -value $\leq .05$ were considered as factors significantly associated with first-line ART treatment failure and the result was presented with a description, graph, and tables. **Results:** In this study, three hundred and fifty peoples were a candidate for the study and all have been involved. The magnitude of first-line ART treatment failure based on virologic criteria was 20.85%. Greater than three-fourth (84.29%) of study participants have support from somebody. Those patients who have initiated first-line ART with NVP based regimen have 1.83 times more likely to face first-line ART treatment failure as compared with those who have started with Efeverence (EFV) based regimen [AOR = 1.83, 95% CI (1.035, 3.245)]. Patients who have initiated first-line ART at the health center were 3.093 times more likely to face first-line ART treatment failure as compared those who have initiated ART at hospitals [AOR = 3.093, 95% CI (1.101, 8.685)]. Patients who have not developed a common opportunistic infection after ART initiation was 47.3% less likely to encounter first-line ART treatment failure as compared with those who have opportunistic infection [AOR = 0.527, 95% CI (0.289, 0.961)]. **Conclusion:** Based on virologic criteria, NVP based ART initiation, having history recorded opportunistic infection after ART initiation, being male, Institution where initiate ART, are significantly associated with the occurrences of first-line ART treatment failure. The action has to be directed on those identified factors to maintain the patient stay on First-line ART by concerned stakeholders.

Keywords

treatment, nevirapine, virologic, antiretroviral, Ethiopia

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Backgrounds

Human Immunodeficiency Virus (HIV) infection is one of the most severe that our world is currently suffering from.¹ The number of people who are taking antiretroviral therapy is increasing from time to time. In 2017, 36.9 million people were living with HIV worldwide in which Africa has two-thirds of those people who are taking Antiretroviral therapy ART.² The magnitude of this ART treatment failure differs from country to country that is the magnitude of virologic based ART treatment failure was 3.6% in Switzerland, 9% in China, and 37% United States of America,³ In Ethiopia, as the 2018 report, the prevalence of people living with HIV/AIDS is 1.15%.⁴

Antiretroviral therapy (ART) is the treatment of people infected with HIV using anti-HIV drugs. It is a combination of drugs (often called “highly active antiretroviral therapy” or HAART) that suppress HIV replication. This combination of drugs will be able to increase potency and reduce virus developing resistance.⁵ In 2017, 79% of patients with HIV infection were accessing ART.⁶

Antiretroviral treatment failure occurs when one group of the regimen is not more effective and the patients shifted to another regimen.⁷ There are three forms by which antiretroviral therapy treatment failure can be confirmed to happen. Those are clinical failure, Immunological failure, and Virological failure.⁷ From those three criteria, the most accepted one is immunologic failure that is CD4 count falls to the baseline (or below) or persistent CD4 levels below 100 cells/mm³ and Virological failure that is said to occur if Plasma viral load above 1000 copies/ ml based on two consecutive viral load measurements after 3 months, with adherence support.⁷ Mostly it is known that virological failure occurs at an earlier stage and is followed by immunological failure, then clinical failure at the end.⁸ These virologic-based criteria indicate the amount of virus in the body, and it is the most accurate to show ART treatment failure. At this time in Ethiopia or as a world, virologic criteria become more effective, and WHO recommends this criterion to determine treatment failure.⁹

Even though ART decreases the rate of death from HIV/AIDS, its treatment failure has become common.¹⁰ At this time, more attention is given to increasing availability/accessibility/ of ART without considering the rising of its treatment failure. As many studies indicated first-line ART treatment failure is high.^{11–14} Systemic review and meta-analysis conducted in Sab- Sahara Africa indicated that the pooled prevalence of ART virologic failure was 15%.¹⁵

Even though Ethiopia uses a differentiated ART service delivery and strategies as early initiation of ART, and strategies of 90-90-90 but still ART treatment failure is high.¹⁶ The Strategies of 90-90-90 was started to implemented in Ethiopia.¹⁷ In Ethiopia, the prevalence of ART treatment failure ranges from 4.9% to 22.7%.^{11,18,19}

In developing counties such as Ethiopia availability of second-line ART is not adequate and second-line ART itself has many negative outcomes on the patient.²⁰ Second-line

ART is more toxic and not convenient for the patients as fixed-dose combinations in first-line ART.²⁰ The available finding indicated that advanced in clinical manifestation, low CD4 counts, and ART drug toxicity are predictors of first-line ART treatment failure.²¹

Many research findings indicated that baseline drug regimen categories, poor ART adherence, high duration on first-line ART, substitution of first-line drug, lost to follow up, recorded drug side effects, and time lag to start ART after diagnosed positive are factors that contribute to ART treatment failure.^{22–26}

Since clinical failure happened at the end of the clinical course, it is better to identify the status of virologic failure before the patients develop an opportunistic infection that hinders the patient to maintain relatively normal health.⁸ So this research was aimed at assessing virologic failure and associated factors among patients taking ART, in order to get ways to maintain the patients to stay on first-line ART for a long period.

Method

Study Design, Period and Setting

A facility -based analytical cross-sectional study was employed. The study was conducted in adult patients with HIV infection who are taking ART at a public hospital located in Southwest Shoa at St. Luke referral hospital and Tulubolo general hospital of central Ethiopia. Both hospitals are located in Oromia regional state in Ethiopia. Those two hospitals are located in the Southwest parts of Addis Ababa, the capital city of Ethiopia.

From both hospitals, St. Luke referral hospital is located in Woliso town which is the capital city of Southwest Shoa zone at 114 km in direction of the Southwest from Addis Ababa. In this hospital ART clinic started in 2006. In 2019 this hospital was giving ART services for a total of 1433HIV adult HIV positive patients. Currently, this hospital is serving around 1.3 million people by having many departments as Clinic for patients with tuberculosis, an ART clinic, an Adult outpatients department, under-five outpatient departments, Antenatal care, Postnatal care, etc During this study, people with HIV positive who were receiving ART were 1563 including children.

Regarding Tulu Bolo general hospital, it started to give service in 2010. It is located in Southwest Shoa at 90km from Addis Ababa. This hospital is currently giving ART for 201 patients with 174 of them are adults with HIV/AIDS, while 27 are less than fifteen years who are treated in a pediatric outpatient department that is different from the adult department.

Sample Size and Sampling Procedure

The sample size for this study was determined using a single population proportion formula. In this case parameters such as 95% confidence level, 5% margin of error were used. The proportion of ART treatment failure used for determining

sample size in this study is 28.5% study conducted in Nigeria.²⁷ The calculate sample size was 313.

Finally, after adding a 12% none response rate, the final sample was 350. Then proportional allocation was computed to get the required number of patients for both hospitals. Accordingly, from St. Luke Referral hospital three hundred and twelve participants have accepted and from Tulu bolo general hospital thirty-eight participants have accepted.

Sapling techniques used to get individual participants in this study was systematic sampling. First, those patients taking ART during the study period were identified by looking at the schedules of the patients from their flow charts. Accordingly, from St. Luke Referral Hospital 560 patients were having the scheduled to take ART during the study period. In one day on average two patients were going to St. Luke Referral Hospital. To identify starting point from either the first coming or the second coming patients, the lottery method was used. According to this lottery, the second coming patient was selected. Then every second patient starting from the second patient on the day of starting data collection was decided to be accepted. Then every second patient was involved in this study until to get 312 patients. Again from Tulu Bolo general 75 patients were having appointments during the data collection period. For this Tulu Bolo general hospital similar method with two intervals was used to get 38 patients in the study period.

Data Collection Tools and Procedures

The tools used in this research were taken from various previously conducted researches^{21,28-32} and ART guideline of Ethiopia, the federal ministry of health, ART follows up forms from the cards, and case manager sheets.²⁰ In this study, the questions are categorized into five parts such as Socio-demographic characteristics of the patients (Sex, Age, Ethnicity, Marital status, Educational status of the patients, Occupation, Religion, and having support), laboratory findings (Baseline hemoglobin), ART treatment-related conditions of the patients (Non-nucleotide reverse transcriptase inhibitors (NNRTI) Based, Lost to follow up, ART adherence status, Disclosure being HIV positive to family/others, the occurrence of drug side effect, Duration on first-line ART, First line ART drug substitution, Time lag to start ART after diagnosed positive, History taking of post-exposure prophylaxis, Suspected route of infection), OI after initiate ART, Chronic non-communicable diseases during on first-line ART, Presence of malnutrition during on first-line ART, Cotrimoxazole taken or not, Mode of first identified ART infection), and questions related with health facilities (Time it asks to go health facilities, Health facility where start first-line ART).

Data Collection Procedure

In this study, three nurses at St. Luke referral hospitals and two nurses at Tulu Bolo general hospitals were assigned for data

collection. Two public health holders were again assigned as supervisors and they have monitored the data collection process at each hospital daily. The questions were accepted from both patients and cards of patients. The medical record number of a patient was reviewed when the patient went to the hospital. The data was collected from both the patients and cards. When the incomplete card or involuntary patient has appeared, the next patient was asked.

Data Quality Assurance

Data were extracted from patient charts /record review/ using a pretested structured checklist. First, the question was translated into the regional language Afan Oromo then it was retranslated back into the English language to maintain the consistence of the questions. The training was given for data collectors and supervisors regarding confidentiality and privacy of data, and how to collect the information from patients and the card. The questionnaires were pretested before the start of the data collection on 18 patients taking ART Amaya hospital. Based on the pretest, questions were revised, edited, and those found to be unclear and that question that couldn't be available were removed. Every continuous variable as BMI was measured to the nearest two decimal places. The world health organization's (WHO) clinical stages and laboratory findings were taken from a card that was recorded during ART initiation. Again another laboratory finding was taken from cards of the patient that is already registered during ART initiation. Based on the pretest, questions were revised, edited, and those found to be unclear and that question that couldn't be available was removed. Supervisors were supervising the data collection process daily. Data completeness was checked daily by the supervisor and principal investigator.

Method of Data Analysis

After checking for completeness, data entry was conducted using Epi Data Version 3 and exported to Stata SE version 14 for analysis. Then descriptive statistics as mean and the percentage was computed. Bivariable logistic regression was used to find covariates significantly associated with first-line ART treatment failure. In this case variables with P -value $\leq .25$ were a candidate for multiple logistic regressions. The backward logistic regression model was used to select the end variables. Finally, variables with P -value $\leq .05$ were considered as factors significantly associated with first-line ART treatment failure and the final finding is presented with a description, graph, and tables.

Ethical Approval and Informed Consent

Ethical clearance was obtained from Debre Markos University of the Ethical review committee of college of health sciences with reference number of dm174/2019. Then Verbal informed consent was obtained from all subjects before the study and

confidentiality of the information was maintained by omitting the names and personal identification.

Result and Discussion

Socio-Demographic Characteristics

Three hundred fifty (350) patients were involved in this study and yielded a response rate of 100%. Greater than half (221 (63.14%)) of the participants' age was greater than 35 years old. Regarding ethnicity around three fourth of them are Oromo 258 (73.71%). Around one-fourth of the participants can't read and write 87 (24.86%). Greater than three fourth 295 (84.29%) of participants have supported from somebody (Table 1).

Clinical Characteristics

In this study, during ART initiation, 147 (42%) participants were at stage I of WHO HIV/AIDS clinical staging (Figure 1).

Regarding baseline body mass index, more than half of the participants (209(59.71%)) were having baseline body mass index of $>18.5 \text{ Kg/m}^2$ (Figure 2).

Table 1. Socio-Demographic Characteristics of Patients Taking ART Drugs at Tulu Bolo General Hospital and St. Luke Referral Hospital.

Characteristics	Options	Frequency	Percent (%)
Sex	Male	166	47.43
	Female	184	52.57
Age	≤ 35 years	221	63.14
	>35 years	129	36.86
Ethnicity	Oromo	258	73.71
	Amara	61	17.43
	Guraghe	27	7.71
	Others	4	1.14
Marital status	Single	40	11.43
	Married	189	54.00
	Separated/ divorced	56	16.00
	Widowed	65	18.57
Education status of the patients	Can't read and write	87	24.86
	Primary	156	44.57
	Secondary	81	23.14
	College and above	26	7.43
Occupation	Farmer	100	28.57
	Employed	45	12.86
	Students	21	6.00
	Merchant	116	33.14
	Laborer	44	12.57
	Others	24	7.00
Religion	Orthodox	222	63.43
	Protestant	101	28.86
	Muslim	27	7.71
Support	Yes	295	84.29
	No	55	15.71

Other * Guraghe, Tigray walayita, Kebene. Other **, driver, carpenter, tailor, police.

During ART initiation, greater than three fourth of the participants (289 (82.57%)) were categorized under working baseline functional status. About (230 (65.71%)) patients were having a baseline opportunistic infection during ART initiation and less than a quarter of the participants (41 (11.71%)) were having chronic non-communicable diseases during ART initiation. Regarding regimen of ART initiation, greater than half (207 (59.14%)) of the patients were initiated first-line ART with Tenofovir (TDF) based Nucleotide Reverse Transcriptase Inhibitors (NRTI). At the first time of ART initiation, (138 (39.43%)) participants have baseline CD4 Counts of greater than 250 cells/ mm³ (Table 2).

ART Treatment Related Condition of the Participants

Two hundred ten (210) 60% patients were initiated first-line ART with Efeverence (EFV) based NNRTI. Regarding having a history of loss to follow up, more than three fourth of the patients (308 (88%)) were having a history of loss to follow up. Again more than half of the participants (199 (56.86%)) have stayed on first-line ART for less than five years (Table 3).

Institution of Taking ART, Laboratory Finding

Regarding the time it asks to go health institution around three fourth of them reach institution in less than one hour 246 (70.29%). Most percent of the participants had initiated ART at the hospitals 331 (94.57%). Around a quarter of the patients (76 (21.71%)) were first confirmed HIV positive by voluntary counseling and testing (VCT) (Table 4).

Factors Associated with Virologic-Based ART Treatment Failure

In this study nineteen variables as sex, having somebody to support, Occurrence of drug side effects, having a history of chronic non-communicable diseases, having a history of first-line ART substitution, base-line body mass index, baseline functional status, base-line opportunistic infection, and kinds of base-line first-line ART regimen have been a candidate for multivariable logistic regression. From those variables, nine variables remained in the final model of which eight of them showed statistically significant association.

The finding showed that the sex of the patients is significantly associated with first-line ART treatment failures. Being females were 52% times less likely to encounter occurrence of first-line ART treatment failures than male participants AOR = 0.48(95%CI, 0.269, 0.856). Regarding the residence of the patients, those who were living in urban were 51.8% less likely faced with the occurrence of first-line ART treatment failure OR = 0.482(95% CI 0.248, 0.937). ART clients those who have started ART at health center/clinic/ were three times more likely to have treatment failure as compared with their counterpart AOR = 3.093(95% CI 1.101, 8.685).

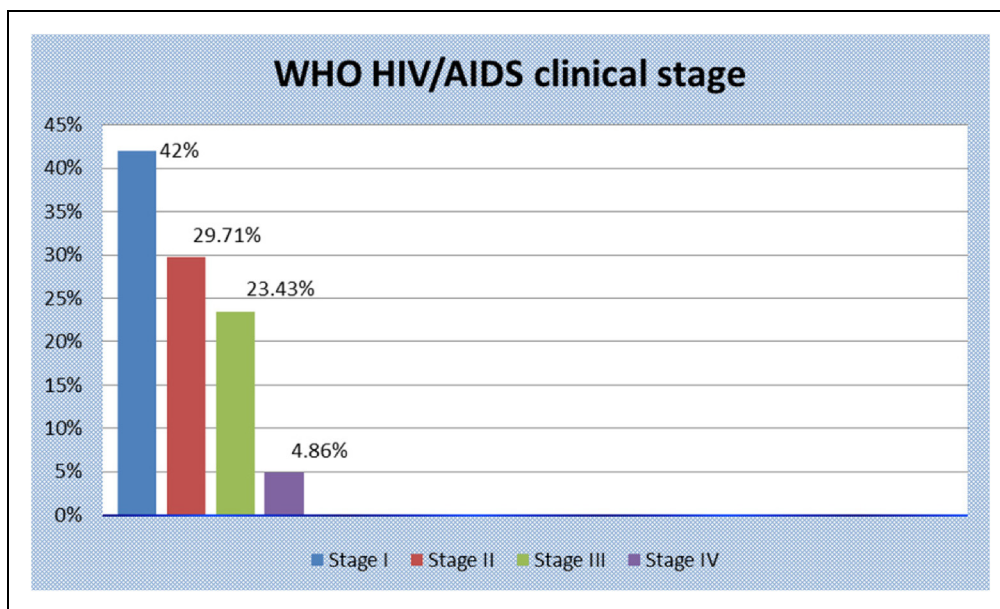


Figure 1. Base line clinical HIV/AIDS stages of participants at Tulu Bolo general hospital and St. Luke referral hospitals.

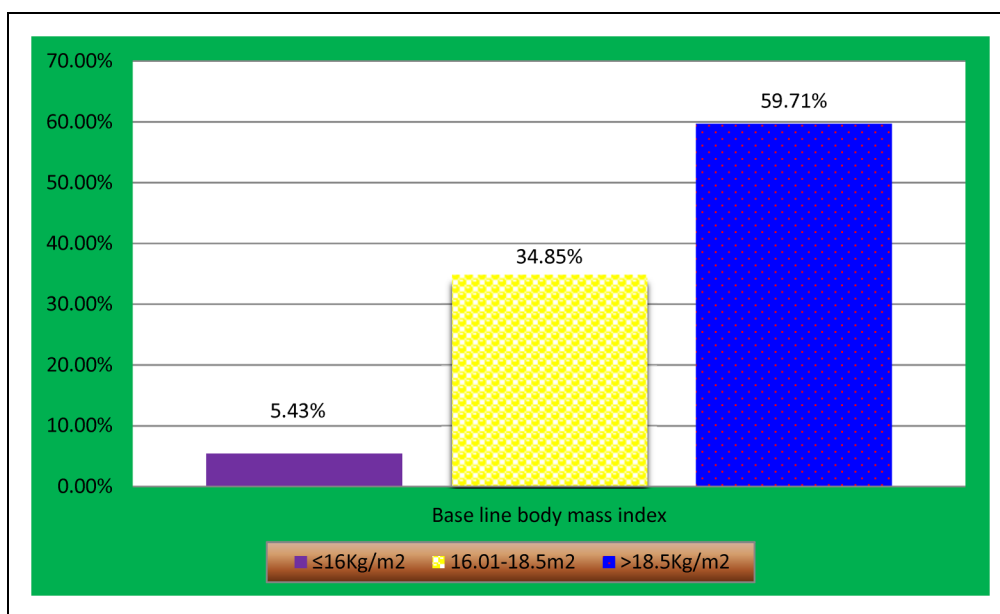


Figure 2. Base-line body- mass index of the participants at Tulu Bolo general hospital and st. Luke referral hospital.

Concerning NNRTI those patients who have initiated first-line ART with NVP based regimen have 1.83 times more likely to face first-line ART treatment failure as compared with those who have started with EFV based regimen OR = 1.83(95%CI 1.035, 3.245). Regarding marital status, those patients who were widowed were 3.309 times more likely to develop early ART treatment failure than those who were single during taking first-line ART AOR = 3.309 (1.073, 10.20). The occurrence of opportunistic infection after ART initiation was significantly associated with first-line ART treatment failure that is those patients who didn't have a common

infection after ART initiation were less likely to encounter occurrence of first-line ART treatment failure by 47.3% (Table 5).

Discussion

First-line ART treatment failure becomes one of the concerning issues in HIV/AIDS treatment. From all criteria of ART treatment confirmation, Virologic failure is the God standard. Regarding the magnitude of ART treatment failure and associated factors, there are no adequate findings. Therefore, the focus

Table 2. Clinical Characteristics the Participants at Tulu Bolo General Hospital and St. Luke Referral Hospital.

Characteristics	Options	Frequency	Percent (%)
Base line functional status	Working	289	82.57
	Ambulatory and bed ridden	61	17.43
Base line opportunistic infection	Yes	230	65.71
	No	120	34.29
OI after initiate ART	Yes	136	38.86
	No	214	61.14
Chronic non communicable diseases during on first line ART	Yes	41	11.71
	No	309	88.29
Presence of malnutrition during on first line ART	Yes	46	13.14
	No	304	86.86
Cotrimoxazole taken or not	Yes	299	85.43
	No	51	14.57

Table 3. ART Treatment Related Condition of the Patients at Tulu Bolo General Hospital and St. Luke Referral Hospital.

Characteristics	Options	Frequency	Percent (%)
NNRTI Based	EFV based	210	60.00
	NVP based	140	40.00
Lost to follow up	Yes	42	12.00
	No	308	88.00
ART adherence status	Good	275	78.57
	Fair	43	12.29
	Poor	32	9.14
Disclosure being HIV positive to family/others	Yes	269	76.86
	No	81	23.14
occurrence of drug side effect	Yes	21	6.00
	No	329	94.00
Duration on first line ART	<=5yrs	199	56.86
	>5yrs	151	43.14
First line ART drug substitution	Yes	92	26.29
	No	258	73.71
Time lag to start ART after diagnosed positive	The same day	51	14.57
	1 to 24 month	273	78.00
	Greater than 24 month	26	7.43

of this study was to find the magnitude of ART treatment failure and associated factors with it in the study area.

This study finding indicated the magnitude of first-line ART treatment based on virologic criteria is 20.85%. This finding is almost similar with study conducted in Dire Dawa another part of Ethiopia.¹⁸ This finding is higher than the study conducted in Tanzania 12.18% and India 16%.¹⁴ The reason behind the difference in this study and Tanzania may be due to the study conducted in Tanzania is being relatively in a recent time that is during 2017 to 2018, but this study finding has included all participants from an early start of the ART treatment. This means, those who have initiated ART in relatively recent years have adequate information regarding ART and they take ART as

Table 4. Institution of Taking ART, Laboratory Findings at Tulu Bolo General Hospital and St. Luke Referral Hospital.

Characteristics	Options	Frequency	Percent (%)
Treatment failed confirmed by Virological criteria	Yes	73	20.85
	No	277	79.14
Time it ask to go health facilities	<=1 h	246	70.29
	>1hrs	104	29.71
Health facility where start first line ART	Hospitals	331	94.57
	Health center	19	5.43
Suspected route of infection	I don't know	66	18.86
	Sexual intercourse	264	75.43
	Sharp material	20	5.71
Mode of first identified ART infection	VCT	76	21.71
	PICT	274	78.29
History taking of Post exposure prophylaxis	yes	9	2.57
	No	341	97.43
Baseline hemoglobin	<10g/dL	17	4.86
	>=10g/dL	333	95.14

expected. Again this finding is lower than a study conducted in the United States of America 10.1%.³³ Furthermore, this discrepancy may be due to differences in education, economic level, and information gap in which Ethiopia is relatively at a lower level in all direction.

Regarding factors associated with First-line ART treatment failure, the findings indicated that initiating first-line ART with NVP is a risk for treatment failure than those who have started with EFV. This finding is consistency with the studies conducted in Johannesburg, South Africa.^{13,34-36} This may be due to high side effect as abdominal pain, rash, headache, vomiting, diarrhea, nausea, fatigue, and muscle pain that is more common in NVP than EFV. Another reason for this is again since EFV is given once a day while NVP is given twice a day that may disturb its adherence status that contributes to treatment failure.

This research finding also revealed that initiating ART at a health center is a risk for ART initiation. This may be due to in health center there being relatively no adequate counseling. In the case of Ethiopia, there are HIV-positive patients who are assigned at hospitals to give counseling services for people who are going to take ART. Those individuals are assigned there for counseling purposes. But, in the health center, there are no such as this services. So it is better if the government assigned those individuals who give counseling at health centers too.

The finding also indicated that being male is a risk factor for first-line ART treatment failure. This research finding is in line with studies conducted in Ethiopia: Jimma town in and Tigray region.^{36,37} This may be due to females are giving more attention to health-seeking behavior than male patients. Farther more, the research finding revealed that being from a rural residence is a risk factor for ART treatment failure. This finding is in line with a study conducted in

Table 5. Bivariate and Multivariate Logistic Regression to Identify Factors Associated with ART Treatment Failure at Tulu Bolo General Hospital and St. Luke Referral Hospital.

Characteristics	First line ART treatment failure		COR (95%CI)	AOR (95%CI)	p-value
	Yes (%)	No (%)			
Sex					
Male	46 (13.1)	120 (34.28)	1		
Female	27 (7.71)	157 (44.85)	0.44 (0.263,0.763)	0.48 (0.269,0.856)	0.013*
Base line opportunistic infection					
Yes	59 (6.85)	171 (48.85)	1		
No	14 (4)	106 (30.28)	0.382 (0.203, 0.719)	0.509 (0.254,1.017)	0.056
Residence of the patients					
Rural	55 (15.7)	182 (52)	1		
Urban	18 (5.14)	95 (27.14)	0.626 (0.348, 1.127)	0.482 (0.248,0.937)	0.031*
Time to initiate ART after confirmed HIV positive					
Within the same day of diagnosis	5 (1.42)	46 (13.14)	1		
After 24 months	62 (17.7)	211 (60.28)	2.703 (1.029, 7.098)	1.587 (0.550,4.578)	0.392
After 24 months	6 (1.71)	20 (5.71)	2.76 (0.753,10.104)	2.303 (0.564,9.399)	0.245
Occurrence of opportunistic infection after ART initiation					
Yes	41 (11.7)	95 (27.14)	1		
No	32 (9.14)	182 (52)	0.407 (0.241,0.688)	0.527 (0.289,0.961)	0.037*
Health facility where start first line ART					
Hospitals	64 (18.2)	267 (76.28)	1		
Health center	9 (2.57)	10 (2.85)	3.754 (1.465,9.621)	3.093 (1.101, 8.685)	0.032*
Base line CD4 level in cells/mm ³					
<50	11 (3.14)	23 (6.57)	1		
50.01-100	12 (3.42)	32 (9.14)	0.784 (0.294,0.84)	0.628 (0.209,1.884)	0.407
100.01-250	31 (8.85)	103 (29.42)	0.629 (0.276, 1.433)	0.759 (0.312,1.844)	0.543
>250	19 (5.42)	119 (34)	0.333 (0.14,0.794)	0.487 (0.189,1.257)	0.137
Marital status					
Single	6 (1.71)	34 (9.71)	1		
Married	37 (10.5)	152 (43.42)	1.379 (0.539,3.528)	1.995 (0.707,5.628)	0.192
separated/divorced	12 (3.42)	44 (12.57)	1.545 (0.526,4.538)	2.299 (0.704,7.507)	0.168
Widowed	18 (5.14)	47 (13.42)	2.17 (0.779,6.041)	3.309 (1.073,10.20)	0.037*
EFV based	33 (9.42)	177 (50.57)	1		
NINRTI Based ART	40 (11.4)	100 (28.57)	2.145 (1.272, 3.616)	1.83 (1.035,3.245)	0.037*

*: Significant association; LFU: lost to follow up; NNRTI: Non nucleotide reverse transcriptase inhibitors; ART: Antiretroviral therapy.

Southwest parts of Ethiopia.³⁶ This may be due to many things as those patients from urban have good knowledge regarding prevention of First-line ART treatment failure as compared from peoples from rural area. Ignoring the command from health care workers is high among rural population. This means person from urban follow the command as it is due to fear of the diseases than peoples from rural and this enhance prevention for First-line ART treatment failure. This may be also due to urban population are eating balanced diet than population from rural area.

In addition to the above findings, this finding also revealed that the presence of opportunistic infection after and before ART initiation is associated with first-line ART treatment failure. This finding is again in line with studies conducted in North East Ethiopia, Dire Dawa, eastern Ethiopia, India.^{18,22,36,38,39} This may be due to the presence of opportunistic infection decreased immunity of the patients that lead treatment failure and also during the presence of this opportunistic infection; the patients may take two drugs at the time that can affect ART by either having drug-drug interaction or making the patients bother to take both medications for co-occurrence of those diseases.

Furthermore, this research finding revealed that NVP based initiation of ART is significantly associated with the occurrence of first-line ART treatment failure. This finding is in line with a study conducted in South Africa.³⁴ It is known that side effects (rash, nausea, fatigue, headache, vomiting, diarrhea abdominal pain, and muscle pain) of NVP are more common and severe than side effects of EFV. This side effect of NVP may be a difficulty for the patient and result in disturbance of ART adherence that leads to first-line ART treatment failure. Again, this may be due to EFV has being recommended to take only one time per day but, NVP is given twice a day and this may contribute happening of adherence disturbance that may lead happening of first-line ART treatment failure.

Conclusion

This study revealed that the prevalence of virologic-based ART treatment failure is high in the study area. For this virologic based first-line ART treatment failure, many contributed factors as starting to take first-line ART with NVP based NNRT, Taking ART at the health center, being from rural residence, presence of opportunistic infection during and after ART initiation are significantly associated with ART treatment failure.

Recommendation

To maintain the patients on first-line ART for long periods of time, it is better to act on those identified factors that contribute to virologic-based ART treatment failure. Those concerned bodies as patients themselves, governments, non-government organizations, and health organizations have to act on those identified factors to maintain the patient on first-line ART for a long period without Treatment failure.

The hospitals have to inform the patients of those identified factors. Counseling the patient must be continuous by a case manager or the health professionals themselves regarding these identified factors for virologic-based ART treatment failure. It is better to know those identified factors for ART treatment failure and give necessary preparation for them and act accordingly. Other strategies have drafted and implemented on the side of the patient. For example, health extension workers have to identify those patients taking ART in the kebele and frequently monitor them by going there house. He /she have to teach on the area: how to prevent opportunistic infection, there must be again more individual home-based teaching for all HIV positive patients.

To those researchers who want to do on this area, it is better to conduct this research by different study designs, areas, and different population

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Authors' Contributions

For this study DM involved in designed, writing result and analysis finding with prepare the manuscript for this research. Again in this study TT participated in analysis of the data while BW, WI and GY were involved in revising this research finding. At the end all authors approved the final manuscript of this research to send for the journals.

Availability of Data and Materials

The source of the data is present whenever at corresponding author. The data can be given to concerned individuals, upon reasonable requested is raised.

Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.


Ethics Approval and Consent

For this research Ethical clearance was obtained from Debre Markos University of the Ethical review committee of college of health sciences in Ethiopia. After formal letter is written to study area data collection was started and verbal consent was obtained from participants to be involved in the study.

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Abbreviations

AOR	NNRTI non- nucleotide reverse transcriptase inhibitors
COR	Crude Odd ratio
ART	Antiretroviral therapy.