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Determinants of Virological Failure among HIV/AIDS Patients on Antiretroviral Therapy in Selected Public Health Facilities in Addis Ababa: A Case Control Study

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Abstract

Background: World Health Organization (WHO) recommends viral load monitoring to ensure viral load suppression is achieved and maintained, there by decreased morbidity and mortality, but large gaps remain particularly in low and middle income countries. Virologic failure and treatment failure remained a major problem in Addis Ababa. Identifying the factors for virologic failure has benefits in controlling transmission and reducing disease burden.

Objectives: To identify the determinants of virologic failure in people living with HIV on antiretroviral therapy in two selected public health facilities in Addis Ababa, Ethiopia

Methods: A hospital based case control study was to identify determinants of virologic failure among HIV/AIDS patients who are on ART in Saint Peter's specialized hospital and Zewditu memorial hospital. A total of 350 participants were recruited with 117 cases and 233 controls with 1:2 ratios of cases to controls. Those who have viral suppression (VL<1000 copies/ml) was taken as controls and those who don't have viral load suppression were classified as cases. Epi info version 7.2.4 and SPSS version 25 were used for data entry and analysis respectively. Bivariate and multivariable regression analysis were conducted to identify factors associated with viral load non-suppression

Results: The majority of the study participants (62.6%) were female while 38.4% were male. Factors associated with viral load non-suppression included younger age (AOR=8.883), disclosure status (AOR=9.123), poor adherence (AOR=21.953), history of chronic disease (AOR=0.14), less duration on treatment (AOR=0.193), 2^{nd} line regimen (AOR=7.611), and treatment failure as a reason for regimen change (AOR=16.381).

Conclusion: Being in the younger age group, poor adherence, long duration on treatment, being on second line regimen were the factors which increase chance of virologic failure. Behavioral intervention to prevent treatment interruption is required to sustain human immunodeficiency virus treatment adherence by focusing on age and treatment duration.

Keywords: Virological failure • Determinants • HIV/AIDS • Poor adherence • Multivariable regression

Introduction

Nearly 38.0 million (31.6 million-44.5 million) people globally were living with human immune deficiency virus in 2019. About 25.4 million (24.5 million-25.6 million) people were accessing antiretroviral therapy in 2019. Around 1.7 million (1.2 million-2.2 million) people became newly infected with HIV in 2019 although new HIV infections have been reduced by 40% since the peak in 1998. The same year, acquired immune deficiency syndrome related mortality has declined by 39% since 2010. In 2019, 81% (68-95%) of people living with HIV knew their HIV status, among these 67% (54-79%) were accessing treatment and 59% (49-69%) were virally suppressed in 2019 [1].

The first evidence of HIV epidemic in Ethiopia was detected in 1984. Since then, HIV/AIDS has claimed the lives of millions and has left behind hundreds of thousands of orphans. The government of Ethiopia took several steps in preventing further disease spread, and in increasing accessibility to HIV care, treatment and support for persons living with HIV. According to the Ethiopian demographic and

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health survey 2016, the national HIV prevalence is 0.9%; the urban prevalence was 2.9%, which is seven times higher than that of the rural (0.4%). The 2016 EDHS also show that the HIV prevalence varies from region to region ranging from less than 0.1% in Ethiopia Somali to 4.8% in Gambella. Furthermore, the 2018 spectrum HIV estimate indicate that the 2017 HIV prevalence in regions ranges from 0.16% to 4.34%.

WHO defines treatment adherences "the extent to which a person's behavior taking medications, following a diet and/ or executing lifestyle changes corresponds with agreed recommendations from a health care provider? For ART, a high level of sustained adherence is necessary to suppress viral replication and improve immunological and clinical outcomes; decrease the risk of developing ARV drug resistance; and reduce the risk of transmitting HIV [2].

The primary objective of antiretroviral treatment is to provide clinical benefits to people living with HIV to achieve long-term durable suppression of HIV replication, which gives immunologic and clinical benefits, and in turn leads to a reduction in morbidity and mortality and improved quality of life. HIV can be suppressed by treatment regimens composed by a combination of 3 or more ARV drugs. Current ART does not cure HIV infection but highly suppresses viral replication within a person's body and allows an individual's immune system recovery to strengthen and regain the capacity to fight off infections. The large scale-up of ART, particularly in low and middle income countries, has resulted in significant gains in health, as well as reductions in HIV related morbidity and mortality. Significant progress has been made on the United Nations 90-90-90 targets. However, there are significant gaps and remaining challenges. WHO recommends viral load monitoring to ensure viral load suppression is achieved and maintained, but large gaps in global access remain, particularly in low and middle income countries and in rural areas [3].

The ability of HIV to mutate and reproduce itself in the presence of antiretroviral drugs is called HIV Drug Resistance (HIVDR). The consequences of HIVDR include treatment failure and further spread of drug resistant HIV. This can compromise the effectiveness of the limited therapeutic options to reach the last 90 target (of achieving viral suppression) and further reduce HIV incidence, mortality and morbidity. Over the last 15 years, scale-up of HIV treatment has had a major impact on HIV related illness, averting AIDS related deaths, preventing new HIV infections, and resulting in cost savings that will contribute to realization of the sustainable development goals. Despite significant advances in the prevention and treatment of HIV, countries continue to experience serious gaps in ART service delivery, including suboptimal retention in treatment and care services, drug stock-outs, suboptimal use of viral load testing, and inadequate support for population adherence to ART, which favors the emergence and transmission of HIVDR [4-9].

According to Ethiopian guidelines routine viral load testing is a more sensitive and early indicator of treatment failure. It suggests viral load testing should be done after 6 and 12 months of initiating ART and then every 12 months then after in order to detect treatment failure proactively. Viral load testing should be used aside from the routine testing schedule whenever there is clinical or immunologic suspicion of treatment failure. Viral load non-suppression is defined as a viral load of >1000 copies/ml anytime though the follow up. When a client is found to have a viral load of >1000 copies/ml on routine or need based viral load test, providers need to address adherence related issues with enhanced support, identification of barriers and addressing them for three months. Viral load testing must be repeated after three months of enhanced adherence support. If the second viral load test is <1000 copies/ml the patient needs to be maintained on the first line regiment ensuring continued adherence support. However, if the second viral load test is >1000 copies/ml, virologic failure is announced and the client need to be switched to appropriate second line regimen based on the first line combination [10-15].

Statement of the problem

The rise in Antimicrobial Resistance (AMR) including HIV drug resistance is one of the greatest threats to global health. If it is not urgently addressed, it may result in millions of deaths, an increase in new and hard to treat infections and increased health-care cost.

Globally, UNAIDS planned to have 90% of people on highly active antiretroviral therapy are virally suppressed by 2020 and end HIV epidemic by 2030; as a result, HIV treatment failure would be prevented. Despite this ambitious goal, as of a systematic analysis of national HIV treatment cascades of 69 countries by 2016, viral suppression was between 7% in China and 68% in Switzerland. According to 2020 UNAIDS global AIDS report only 59% of people living with HIV have viral suppression [16].

A higher viral load is the main indicator of HIV treatment failure, which is becoming a threat across different African countries, for instance virological failure is reported to be 14.9% in Tanzania and 9% according to a study done in Kenya, Uganda, Tanzania and Nigeri.

When we see the predictors of virologic non-suppression and virological failure, lower $CD4^+$ T-cell count ($P<0.01$), non-adherence to ART ($P<0.01$) and drug resistance mutations were present in 87/115 samples (75.7%), as well as being on second line, low CD4 count, missing any day of ART and history of fever in the past week remain important predictors of virologic failure. The study done in Addis Ababa also found out CD4 count with cutoff point 50 cells/ mm^3, missed appointments with cutoff point 3 days per month, drug (HAART) substitution, baseline functional status, weight at baseline, WHO stage at baseline, status at last visit, and disclosure status and the multivariate cox analysis identified five significant predictors of treatment failure; which were years since HIV diagnosis, disclosure, WHO stage at start, weight at baseline, and status at last visit.

From the above findings, we can see the haphazard data of virological failure which almost all of them shows high figure in different areas, whereas no single study done on determinants of viral load non-suppression before patients go into full blown failure which might be helpful in tackling the problem early. On another stance there is no study done in study area which shows determinants of viral load non-suppression [17-20].

On top of this even if different recommendation were forwarded from above studies, it is difficult to use them directly as they are done in different set ups and may not work in study area.

Therefore, identifying and managing determinants of virological non-suppression are of paramount importance to achieve a high treatment success rate and improve the quality of life and add significant value for achievement of the virologic suppression.

However, there is limited evidence on the determinants of virological non-suppression among HIV-infected patients on HAART in Ethiopia and in the study area particularly. Thus, this study was aimed to identify the determinants of virological non-suppression among HIV infected patients on ART and will help as an input in an effort towards achievement of the 90-90-90 goal.

Materials and Methods

Study setting and participants

A case control study was conducted at Saint Peter specialized hospital and Zewditu hospital which are located in Addis Ababa and providing a comprehensive HIV care and treatment in Ethiopia. Cases were all HIV patients aged 5 years old attending ART clinic of SPSH and ZMH whose viral load is ≥ 1000 copies/ml that fulfills inclusion criteria's which are enrolled to treatment. Controls were all HIV patients aged 5 years attending ART clinic of SPSH and ZMH whose viral load is ≤ 1000 copies/ml that fulfills inclusion criteria's which is enrolled to treatment.

All patients who are lost to follow-up or transfer in and dropout with inadequate data were excluded from the study. The study was conducted from December 15/2020 to February 15/2021.

Sample size and sampling technique

Sample size was determined using Epi Info™ Version: 7.0 StatCalc by considering 95% confidence level, 80% power, control to case ratio of 2:1, taking the key predictor of virological failure (WHO stage 3 and 4 which gave the largest sample size among the variables) from a previous study in Harar public hospital with AOR=2.04, which gave us total sample size of 318. Taking 10% non-response rate actual sample size will be 350 subjects, making 117 cases and 233 controls.

Sampling technique and procedures

Source population were identified first from ART unit register and smart care of both hospital ART clinic based on exclusion and inclusion criteria. Then eligible participants were selected using simple random sampling technique. Forty percent of study participant for both case and controls were taken from SPSH (140 total=47 cases and 93 controls), while the other 60% were taken from Zewditu Hospital (210 total=70 cases and 140 controls). The total sample is allocated to the two health facilities proportionally according to the number of patients.

Data collection procedures

Data were extracted from patient charts/record review using a pretested structured checklist. Charts were reviewed and participant demographic and clinical characteristics manually abstracted from a standardized ministry of health HIV clinical encounter form completed at each clinic visit. Initial routine viral load result was defined as most recent viral load received between Jan 01/2019 and Jan 01/2020. After the initial viral load result patient charts were reviewed for subsequent viral load testing and clinical data. Data were extracted by a trained professional. Adherence to treatment was determined using the World Health Organization (WHO) definition as used in the follow-up chart.

Data analysis

Data were entered into Epi Info version 7 and were analyzed using SPSS version 25. Descriptive statistics, including mean values and frequencies, were used to describe demographic, clinical, and medication related characteristics of patients. All variables potentially associated with failure to achieve viral suppression were explored. Bivariate and multivariable logistic regression models were then fitted to identify predictors of failure to suppress at first and subsequent testing and to obtain measures of association in the form of Odds Ratios (OR) and 95% Confidence Intervals (CI). Bi-variate analysis was carried out for all independent variables with an outcome variable. Variables with a p-value of less than 0.25 during bivariate analysis were selected as a candidate variables for a multivariable logistic regression. A p-value of less than 0.05 was considered as a cut off to declare statistical significance. Goodness of fit of the model was also assessed using Hosmer and Lemeshow and classification accuracy rate. Hosmer and Lemeshow test statistics (*Chi-square*=8.99, P=0.343) indicates well-fitting model. Similarly, classification accuracy rate for the final model was 88.1%. Multicollinearity was checked between variables using collinearity statistics (Tolerance and VIF) and no multicollinearity was detected.

Results

Sociodemographic characteristics

A total of 350 eligible subjects were enrolled, 117 cases (those with VL>=1000 copies/ml) and 233 controls (those with VL<1000 copies/ml). Two hundred ten (60%) participants were from clients attending ART clinic of Zewditu Memorial hospital and one hundred forty (40%) are from clients attending ART clinic of Saint Peter specialized hospital.

A majority, 219 (62.6%), of the participants were females and 70.9% of the cases and 54.1% of controls were in the age category of 15-39 years with the rest being above or equal to 40 for both groups. The study also indicates one hundred nine (93.2%) cases and two hundred eleven (90.6%) of the control subjects are from urban area while the rest constitutes rural areas. The study also identified forty-nine (41.9%) cases and eighty-eight (37.8%) controls were unemployed with fairly similar number (41.9%) of cases and (46.7%) controls were employed (Table 1).

Variable	Categories	Cases no. (%)	Controls no. (%)
Sex	Female	67 (57.3%)	152 (65.2%)
	Male	50 (42.7%)	81 (34.8%)
Age	15-24	35 (29.9%)	19 (8.2%)*
	25-34	25 (21.4%)	59 (25.3%)

	35-44	35 (29.9%)	80 (34.3%)
	45 and above	22 (18.8%)	75 (32.2%)
Residence	Urban	109 (93.2%)	211 (90.6%)
	Rural	8 (6.8%)	22 (9.4%)
Marital status	Unmarried	60 (51.3%)	72 (30.9%)
	Married	29 (24.8%)	78 (33.5%)
	Divorced	21 (17.9%)	45 (19.3%)
	Widowed	7 (6.0%)	38 (16.3%)

*Variables which show significant association during the bivariate analysis at P<0.25

Table 1. Socio-demographic characteristics and virological status of the respondents attending ART clinics in Zewditu memorial hospital and Saint Peter specialized hospital Addis Ababa, Ethiopia, (n=350), 2021.

Clinical characteristics

Eighty-two (70.1%) cases and one hundred seventy-one (73.4%) controls have a normal body mass index ranging from 18.4 to 24.9 kg/m^2 while a quarter of (26.5%) cases and fifty-eight (24.9%) of controls are undernourished, and four (3.4%) cases and four (1.7%) controls have a body mass index above 25 kg/m^2. Concerning disclosure status, majority (86.3%) of cases and (81.1%) controls have disclosed status.

Nearly a half (49.6%) of cases and a quarter (25.3%) of controls have been on treatment for more than or equal to ten years whereas thirty-three (28.2%) and eighty-six (36.9%) of controls were on treatment for about five to nine years. A baseline opportunistic infection have been also assessed and 53 (45.3%) of cases and 100 (42.9%) of controls have some form of opportunistic infection at the start of the treatment and tuberculosis of any type takes the greater share of the baseline opportunistic infections (Table 2).

Variables	Categories	Cases no. (%)	Controls no. (%)
Baseline BMI	=<18.4	31 (26.5%)	58 (24.9%)
	18.5-24.9	82 (70.1%)	171 (73.4%)
	>=25	4 (3.4%)	4 (1.7%)
Current functional status	Working	103 (88.0%)	218 (93.6%)*
	Ambulatory	11 (9.4%)	14 (6.0%)
	Bed ridden	3 (2.6%)	1 (0.4%)
Disclosure status	Disclosed	101(86.3%)	189 (81.1%)*
	Non disclosed	13 (11.1%)	6 (2.6%)*
	Unknown	3 (2.6%)	38 (16.3%)
Duration on Rx	<1 year	4 (3.4%)	5 (2.2%)
	1-4 years	22 (18.8%)	83 (35.6%)
	5-9 years	33 (28.2%)	86 (36.9%)*
	>=10 years	58 (49.6%)	59 (25.3%)*
WHO stage	Stage I on Rx	106 (90.6%)	225 (96.6%)
	Stage II on Rx	3 (2.6%)	3 (1.3%)
	Stage III on Rx	3 (2.6%)	1 (0.4%)
	Stage IV on Rx	5 (4.3%)	4 (1.7%)
Baseline OI's	Yes	53 (45.3%)	100 (42.9%)
	No	64 (54.7%)	133 (57.1%)
Any known chronic illness	Yes	11 (9.4%)	37 (15.9%)*
	No	106 (90.6%)	196 (84.1%)

*Variables which show significant association during the bivariate analysis at P<0.25

Table 2. Clinical characteristics and virologic failure among ART patients attending Saint Peter specialized hospital and Zewditu memorial hospital, Addis Ababa, Ethiopia, (n=350), 2021.

Adherence to ART medication have been evaluated as well. Sixty-one (52.1%) of cases and two hundred twenty-two (95.3%) of the controls have a good adherence to their ART medication while, fifty-six (47.9%) of cases and 11 (4.7%) have poor adherence (Figure 1).

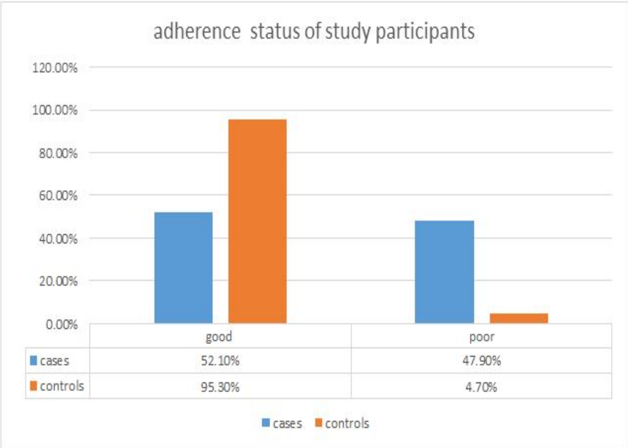

Figure 1. Adherence status and virological status of the respondents attending ART clinics in Zewditu memorial hospital and Saint Peter specialized hospital Addis Ababa, Ethiopia, (n=350), 2021.

Drug and regimen characteristics

More than 3/4th of the participants were on first line while the remaining was on 2nd line ART where 53 (45.3%) cases and 219 (94%) controls were on the first line treatment. Almost all, 327, participants had a history of ART regimen change throughout their follow up and management period. As indicated in the Table 3 below, one hundred eleven (94.9%) cases and two hundred sixteen (92.7%) controls had history of ART regimen change throughout their follow up. The two major reasons for regimen change are new drug availability throughout the course and treatment failure, among other reasons. The study also assessed the reason for regimen change. The major reason for treatment change was treatment failure (50.9%) and new drug availability (73.1%) for cases and controls respectively (Table 3).

Variables	Categories	Cases no. (%)	Controls no. (%)
Current regimen	1st line	53 (45.3%)	219 (94%)
	2nd line	64 (54.7%)	14 (6%)*
History of regimen change throughout management	Yes	111 (94.9%)	216 (92.7%)
	No	6 (5.1%)	17 (7.3%)
Taking other drug in addition to ART	Yes	64 (54.7%)	84 (36.1%)*
	No	53 (45.3%)	149 (63.9%)
If yes, how many (type)	1-2	49 (76.6%)	74 (88.1%)
	3 and above	49 (76.6%)	10 (11.9%)

*Variables which show significant association during the bivariate analysis at P<0.25

Table 3. Drug characteristics and virologic failure in ART patients attending Saint Peter specialized hospital and Zewditu memorial hospital Addis Ababa, Ethiopia, (n=350), 2021.

Immunological factors

The baseline CD4 count of the majority of the participants was in the range of 50-199 cell/mm^3 at the start of their treatment and follow up. As one can see from the Table 4 below sixty-eight (58.1%) of cases and one hundred nineteen (51.1%) of the controls had a CD4 count in the range of 50-199/mm^3 at the start of the treatment.

Twenty one (17.9%) cases and twenty nine (12.4%) controls had a baseline CD4 count below 50/mm^3. In addition, 117 (100%) of cases and twenty (8.6%) of controls had VL copies above 1000/ml at least once throughout their follow up. Among these, thirty nine (33.3%) of cases and twelve (60%) of controls had VL below 1000 copies/ml in their subsequent 3 months follow-up.

Variables	Categories	Cases no. (%)	Controls no. (%)
Baseline CD4 count	<50	21 (17.9%)	29 (12.4%)
	50-199	68 (58.1%)	119 (51.1%)
	200-499	25 (21.4%)	71 (30.5%)
	500 and above	3 (2.6%)	14 (6.0%)
VL >=1000 copies/ml throughout the follow-up	Yes	117 (100%)	20 (8.6%)
	No	0 (0.0%)	213 (91.4%)
if yes, subsequent 3rd month VL result	<1000 copies/ml	39 (33.3%)	12 (60%)
	>=1000 copies/ml	58 (49.6%)	8 (40%)
	undetermined	20 (17.1%)	0 (0.0%)

Table 4. Biochemical characteristics and virologic failure in ART patients attending Saint Peter specialized hospital and Zewditu memorial hospital Addis Ababa, Ethiopia, (n=350), 2021.

Factors independently associated with virological failure

During bivariate analysis, sex, age, marital status, educational status, functional status, disclosure status, duration on treatment, adherence to treatment, WHO stage, presence of known chronic illness, current regimen, reason for regimen change, taking other medication, and baseline CD4 status of the respondents exhibited association with virological failure at $P<0.25$ and were found to be candidate variables for the final model. During multivariable logistic regression analysis, a P value of <0.05 was used to declare statistical significance.

Goodness of fit of the model was also assessed using Hosmer and Lemeshow and classification accuracy rate. Hosmer and Lemeshow test statistics (*Chi-square*=8.99, P=0.343) indicated fitting model. Similarly classification accuracy rate for the final model was 88.1%. Multicollinearity was checked between independent variables using collinearity statistics (Tolerance and VIF) and no multicollinearity was detected.

Age is the only significant independent predictor of high viral load status from sociodemographic factors. The study revealed that individuals who are 15-24 years of age are at almost 9 times more risk of developing virological failure compared to those who are aged 45 and above (AOR=8.883; 95%CI: 2.085- 37.846; P=0.003).

The study shows that the individuals who have disclosed their status to their closed ones are 9 times more prone to develop high viral load compared to those whose status of disclosure are unknown (AOR=9.123; 95% CI: 1.297-64.142; P=0.026). It is also seen that those clients who have poor adherence to ART regimen have 21 times more likely to develop high viral load when compared to those who have good adherence (AOR=21.953; 95% CI: 6.513-71.583; P=0.000). Having a known chronic disease is protective from having high virologic status when compared to those who doesn't have known chronic disease (AOR=0.14; 95% CI: 0.036-0.545; P=0.005).

Similarly, duration on treatment also turned out to be another significant independent predictor of high viral load status. Accordingly, being on ART regimen for less than five years is protective of having high viral load when compared to those who have been on treatment for more than or equal to ten years (AOR=0.193; 95% CI: 0.067-0.550; P=0.002).

The study found out that those who are on second line ART regimen has 7 times more risk of having high viral load when compared to those who are on first line ART regimen (AOR=7.611; 95% CI: 1.725-33.576; P=0.007). In addition, regimen change is also an independent risk factor for having high viral load status. Those clients who changed their regimen due to treatment failure has 16 times more chance of developing high viral load when compared to those who changed due to other reasons (AOR=16.381; 95% CI: 2.246-119.454; P=0.006). In addition, those who had regimen change due to new drug availability during the treatment course has 6 times more likely to have high viral load when compared to those who changed their regimen due to other cases (AOR=6.974; 95% CI: 1.327-36.665; P=0.022) (Table 5).

Variable	Categories	Cases no. (%)	Controls no. (%)	COR (95% CI)	AOR (95% CI)
Age	15-24	35 (29.9%)	19 (8.2%)	6.2 (3.01-13.07)	8.883 (2.085- 37.846)*
	25-34	25 (21.4%)	59 (25.3%)	1.4 (0.74-2.8)	2.635 (.852 - 8.143)
	35-44	35 (29.9%)	80 (34.3%)	1.4 (0.80-2.77)	1.778 (.604- 5.235)
	45 and above	22 (18.8%)	75 (32.2%)	1.00	
Disclosure status	Disclosed	101 (86.3%)	189 (81.1%)	6.769 (2.03-22.47)	9.123 (1.297- 64.142)*
	Non disclosed	13 (11.1%)	6 (2.6%)	27.444 (5.98-125.76)	5.207 (.410- 66.210)

	Unknown	3 (2.6%)	38 (16.3%)	1.00	
Adherence status	Good	61 (52.1%)	222 (95.3%)	1.00	
	Poor	56 (47.9%)	11 (4.7%)	18.528 (9.148-37.526)	21.593 (6.513-71.583)*
Any known chronic illness	Yes	11 (9.4%)	37 (15.9%)	.55 (0.26-1.12)	.140 (0.036-0.545)*
	No	106 (90.6%)	196 (84.1%)	1.00	
Duration on treatment	<1 year	4 (3.4%)	5 (2.2%)	0.814 (0.208-3.183)	2.230 (0.292-17.039)
	1-4 years	22 (18.8%)	83 (35.6%)	0.270 (0.149-0.488)	0.193 (0.067-0.550)*
	5-9 years	33 (28.2%)	86 (36.9%)	0.390 (0.227-0.670)	0.418 (0.158-1.102)
	>=10 years	58 (49.6%)	59 (25.3%)		
Current regimen	1st line	53 (45.3%)	219 (94%)	1.00	
	2nd line	64 (54.7%)	14 (6%)	18.889 (9.847-36.237)	7.611 (1.725- 33.576)*
Reason for regimen change	Treatment failure	57 (50.9%)	13 (6.0%)	65.769 (17.661-244.929)	16.381 (2.246-119.454)*
	New drug available	52 (46.4%)	158 (73.1%)	4.937 (1.472-16.555)	6.974 (1.327-36.665)*
	Other	3 (2.7%)	45 (20.8%)	1.00	

*Variables which show significant association during the multiple logistic regression at P<0.05

Table 5. Factors independently associated with virologic failure in ART patients in Saint Peter specialized hospital and Zewditu memorial hospital Addis Ababa, Ethiopia, (n=350), 2021.

Discussion

Preventing and managing the emergence of HIVDR is a key component of a comprehensive and effective HIV response and actions to monitor, prevent and respond to HIVDR are implemented at the clinical, programme and policy levels to address the many drivers of HIVDR.

High viral load and virologic failure are one of the main challenges especially in developing countries. Multiple studies done in different set up shows very high prevalence of virologic non-suppression with related to many different factors; however, the degree and cause of the problem differ from country to country. For instance, the viral non-suppression rate in South Africa is 15%, Mozambique 24%, Uganda 11%. The magnitude of viral load non-suppression in Ethiopia remain very high which was 15.9% from meta-analysis done by Endalelaw and colleagues. This value is very high when compared to UNAIDS 2030 95-95-95 target but it varies across regions. To mention some from facility based cross sectional study done in Jimma, it shows high viral load status prevalence is 20.3%, 14.7% in Gonder, 11.5% in Tigray region, 1.3% in Addis Abeba, 10.7% in Bahrdar and 21% in Harar.

Age was found to be a significant risk factor of high viral load status in PLWHAs on ART in this study. The study revealed that individuals who are 15-24 years of age are at 7 times more risk of developing virological failure compared to those who are aged 45 and above (AOR=8.883; 95% CI: 2.085- 37.846; P=0.003). This finding is in accordance to a study done in Northern Ethiopia Uganda and Mozambique. In addition another study done in Tigray region of Ethiopia suggests age <40 as a significant predictor of high viral load status even if the exact age category in this group doesn't match with age category in this study. Another study done in Swaziland also mentioned children and adolescents have more risk of high virologic failure when compared to that adult age group. Similarly, a study conducted in the USA discussed that older patients were more likely to achieve viral suppression. A lot of factor could be the potential reasons for this including schooling environment (for those in schools), transition to adolescent and young adults, stigma, fear of disclosure, and stress may affect younger people more than their older counterparts. Alcohol use, drug use for recreational purposes, and low socioeconomic status may also contribute to non-adherence and hence virological failure among the young people. Even though being unmarried (P=0.001) and having no formal education (P=0.029) shown to be risk factors for high viral load status among PLWHAs on ART in bivariate analyses, it exhibited no significant association during multivariable analyses.

The study shows that the individuals who have disclosed their status to their loved ones are 9 times more prone to develop high viral load status when compared to those whose status of disclosure are unknown. In contrast to this study, other studies reported disclosure as a protective factor against high viral load. However the possible explanation for our finding could be due to the fact that individuals might face stigma due to their known status, loss of sexual/romantic partners, emotional harming of family/friends, shattering of privacy, physical isolation, blame, and loss of income which one way or other will affect the patients adherence and follow-up of their ART which in turn lead to high viral load status. Another reason might be due to the association of HIV status disclosure with clinical stage of disease. Individuals on the early clinical state (stage I and II) of the WHO stage of disease were 78% less likely to disclose to a partner compared to those in an advanced (Stages III and IV) state of disease.

The study also indicated that those clients who have poor adherence to ART regimen have 21 times more likely to develop high viral load when compared to those who have good adherence (AOR=21.953; 95% CI: 6.513-71.583; P=0.000). These findings coincide with multiple studies and another metanalysis study done in Ethiopia also pointed out as having poor adherence as an independent significant risk factor for having high viral load and subsequent treatment failure. This is because, as the drug concentration decreases in the blood, HIV RNAs might not be suppressed which in turn leads to increase in viral load.

Duration on ART also shown to be the significant risk factor for having high viral load. Accordingly, being on ART regimen for less than five year is protective of having high viral load when compared to those who have been on treatment for more than or equal to ten years. This finding is supported by other similar studies where longer treatment duration is indicated as one of the significant risk factor for developing high viral load status and virologic failure. The reason for failure among those could be associated with diminished immunity due to age and long stay on treatment, high risk of developing drug side effects and resistance easily. In addition, as duration of treatment increases the probability of being non-adherent might also increase.

The study indicated having a diagnosed chronic disease is protective from developing virological failure. This finding is supported by studies done to understand relation of comorbid conditions and viral load suppression. In a study done by Fischetti and Colleagues, they found out as number of comorbid conditions increase risk of having high viral load decreases. Study done in South Africa, found no association between a detectable HIV viral load and NCD comorbidity. The reason may be the enhanced care given to the patients with multiple comorbid condition which may synergistically support patient wellbeing and viral load suppression. On top of that patient with comorbid condition may have better self-awareness and be more adherent to their medication and follow-up.

On the other hand, the study found out that those who are on second line ART regimen has more risk of having high viral load when compared to those who are on first line ART. Similar study done in northern Ethiopia also indicated that being on second line put patients on more risk of having high viral load. Another study done in Ethiopian on patient taking Dolutegravir based first line management showed that Dolutegravir based regimen maintains high virological suppression which supports these study findings. The reason might be more drug side effect with second line, less tolerability, more pill burden, the initial problem which lead to treatment failure may not be solved as well.

Coming to reason for regimen change, those clients who changed their regimen due to treatment failure has 16 times more chance of developing high viral load when compared to those who changed due to other reasons. This could be due to the fact that who had developed treatment failure will be managed with 2nd line or 3rd line ART regimen which is less tolerable to patients. The initial reason for failure may not also be solved during the regimen change leading to more drug side effect which in turn leads to less adherence to thechange due to new drug availability during the treatment course have 6 times more likely to have high viral load when compared to those who changed their regimen due to other cases. No study found to support this but it could be due to patient intolerance to the new drug as well.

The study finding might be limited by the use of secondary data including lack of some important information such as behavioural factors and income.

Conclusion

In summary, this study identified potential factors that facilitate the development of virologic failure among peoples living with HIV/AIDS on ART which may inform possible interventions to prevent virologic failure. Young age, disclosure status, poor adherence to ART regimen, known chronic disease, long duration on treatment, being on 2nd line regimen and treatment failure as a reason for regimen change are independent factors associated with virologic non-uppression. Early identification of virologic failure allows patients to have a higher chance of success when switching to a second-line or third line ART and also help to prevent inappropriate drug switches. More importantly early identification and management of the possible risk factors would have an important impact on patient lives and as well as ART service in general.

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Ethical Considerations

Institutional ethical clearance was obtained from the Saint Paul millennium medical college, ethical review board. Furthermore, permissions were obtained from respective hospitals for undergoing the study. Each data was kept confidentially using codes and the collected data were kept safe throughout the whole process of the research work to limit data accessibility to a third party.

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