



Determinants of Virologic failure among HIV/AIDS patients on Antiretroviral Therapy in selected Public Health facilities in Addis Ababa: A case control study

Graduate study program

School of Public Health

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Addis Ababa, Ethiopia

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Abstracts

Background: -. World Health Organization recommends viral load monitoring to ensure viral load suppression is achieved and maintained, thereby 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. So, this study tries to identify the risk factors of virologic failure and will be an input in proper management and prevention strategy of high viral load status and subsequent treatment failure in patients on ART.

Objectives: - to assess 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 conducted from 15-december/2020 to 15-february/2021 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 enrolled of which 117 cases and 233 controls in the study with 1:2 ratios of cases to controls. Those who have viral suppression (VL < 1000 copies/ml) were taken as controls and those who don't have viral load suppression were classified as cases. Data extracted from patient charts using a pre-tested structured checklist by trained health professionals. Epi info version 7.2.4 and SPSS version 25 were used for data entry and analysis respectively. Odds ratio with 95% confidence interval were used to identify associated variables at P-value of ≤ 0.05 . Bivariate and multivariable regression analysis were used to determine the independent associated factors.

Results. Age 15-24 (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), 2nd line regimen (AOR =7.611), treatment failure as a reason for regimen change (AOR=16.381) were found to be the potential risk factors of viral load non-suppression among People living with HIV/AIDS on antiretroviral treatment.

Conclusion. Being young age group, poor adherence, long duration on treatment, 2nd line regimen were the factors which increase chance of virologic factors. HIV intervention programs need to address the specified contributing factors. Behavioral intervention to prevent treatment interruption is required to sustain human immunodeficiency virus treatment adherence.

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Acronym's

AIDS:	Acquired Immune-Deficiency Syndrome
ART:	Antiretroviral Therapy
BMI:	Body Mass Index
CDC:	Center for Disease Control
CD4:	Cluster Differentiation 4
DPH:	Department of Public Health
EDHS:	Ethiopian Demographic Health Survey
FMOH:	Federal Ministry of Health
HAART:	Highly Active Antiretroviral Treatment
HIV:	Human Immune Deficiency Virus
LMIC:	Low- and Middle-Income Countries
SPSH	saint Peter Specialized Hospital
PDR:	Primary Drug Resistance
PLWHIV:	People Living with HIV Aids
RNA:	Ribo-Nucleic Acid
UNAIDS:	United Nations
VL:	Viral Load
WHO:	World Health Organization
ZMH	Zewditu Memorial Hospital

1. Introduction

1.1. Background of the study

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 Health Survey 2016 (EDHS 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% (2).

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(3).

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 (4). 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.

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).

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 & 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 >1000copies/ml anytime though the follow up. When a client is found to have a viral load of >1000copies/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 <1000copies/ml the patient need to

be maintained on the first line regimen 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(5).

1.2.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(6).

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 (7). 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(8) .According to 2020 UNAIDS global AIDS report only 59% of people living with HIV have viral suppression (9).

A higher viral load is the main indicator of HIV treatment failure, which is becoming a threat of different African countries, like in Tanzania (14.9%)(10). Another African cohort study including participants from Kenya, Uganda, Tanzania and Nigeria conducted in 2019 showed that 9% of virological failure (11),(12).

In Ethiopia, virological failure is found in the range between 1.3% in Addis Ababa(13) to 11.5% in Tigray(14) to 24% in Gonder(15) and 10.5 in Amhara[(14), (16)]. Another study done in Harar public hospitals to assess prevalence of first-line antiretroviral treatment failure found it to be 21%(17). According to a study in Felegehiwot Referral Hospital in Amhara Region, since HAART was started, 51.1% of study participants have encountered virological failure within 6–48 months (16). From meta-analysis done in 2020 to understand the national burden of virologic failure because of disparity in findings, the pooled prevalence of virologic failure from six studies with a total of 2406 participant shows 5.6% (95% CI: 2.9–8.3%). (18).A retrospective study conducted in public hospitals in Addis Ababa showed that magnitude of ART treatment failure is 19.8% of which 15, 6.3 and 1.3% is immunological, clinical and virological failure respectively(13).

When we see the predictors of virologic non-suppression and virological failure, lower CD4+Tcell count ($P=0.01$), non-adherence to ART ($P=0.01$) and drug resistance mutations were present in 87/115 samples (75.7%)(10), as well as being on second line, low CD4 count, missing any day of ART and history of fever in the past week [(11),(12)]remain important predictors of virologic failure. The study done in Addis Ababa also found out CD4 count with cutoff point 50 cells/mm³ , 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(13).

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.

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.

So 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 aims to identify the determinants of virological non-suppression among HIV-infected patients on HAART at study areas and in the meantime will be a very good asset toward achievement of the 90-90-90 goal.

1.3. Significance of the study

Even though more than 20,000 patients get care at Saint Peter Specialized Hospital's ART clinic and Zewditu memorial Hospital , and also more than 6000 of them are currently on ART in both setups, there is continuous increment in treatment failure rate and requirement for second line ART is growing from time to time. Multicenter retrospective follow-up study conducted in northwest Ethiopia indicated that the incidence of first line ART treatment failure is 61.7 per 1000 person years of observation(19).

A retrospective cohort study done on 595 study participants in Zewditu memorial Hospital, showed 465(78.5%) were right censored (free of treatment failure). It was found that a total of 128 study participants (21.5%) have indication of treatment failure with the occurrence rate was 4.91cases per 1000 months follow up paired. Among the total 128 treatment failures 15.3%, 1.8% and 4.4% individual were categorized immunological, virological and clinical respectively (20).

Occurrence of first line ART failure has many negative out comes. As the research findings shows, drug resistance will be increased after patient shifted second line ART (NNRTIs65.5%, NRTIs, 53.3%, PIs 1.1%) (21). Drug on regimens of first line are simpler to use, less toxic and more convenient as fixed-dose combinations than second line ART (5).

Other research also showed that early mortality, drug toxicity and resistance is high in second line ART (22). Another finding also indicates the chance of viral suppression is low and death is high after first line ART treatment failure (23).

So the result of the study will be expected to give an insight to in addressing factors associated with virological failure. And also the result will have paramount importance in trying to end the pandemic by the 2030. The study will try to dig out key intervention areas to tackle factors associated with virological failure, so that patient stays on first line for longer duration of time and prevent treatment failure. As a result the virologic failure will be minimized and mortality and morbidity associated with it will be reduced which will have significant effect in improving ART patients quality of life in general.

2. Literature review

2.1. Overview of viral load non suppression

People living with HIV infection require ongoing HIV care and access to medications to prevent virological non- suppression, allow immune reconstitution, minimize the risk of resistance emergence, prevent HIV-related morbidity and mortality, and prevent transmission of drug resistant HIV mutations(24).

The World Health Organization (WHO) recommends, where possible the VL of individuals receiving ART be measured every 6 months to detect viral replication and confirm treatment failure. In Low and Middle- Income Countries (LMICs), an elevated or non-suppressed VL Ribonucleic Acid (RNA) copies (> 1000 copies/ml in plasma) in a patient who has been on ART for at least six months(13) is an evidence of failing viral suppression or rebound (7). According to the 2020 UNAIDS global AIDS report, virological suppression stands only at 59% which shows a long way to go to achieve goal for 2030 to end the pandemic(1).

Virological failure, which is a more informative treatment failure, is a common problem that an HIV patient faces after starting treatment. Current guidelines recommend that once patients start treatment, virological failure should not exceed 10% (7). However, studies show that virological failure is much higher than expected and viral replication continues to be a major challenge among patients living with HIV (25).

So here below, I will review literatures exhaustively on determinants of virologic non suppression thoroughly.

2.2. Factors affecting viral load non-suppression

2.2.1. Socio-demographic and socio-economic factors

A study done in Asian continent involving those < 20 years of age from six countries trying to compare early and late virologic failure and factors associated with it. Factors at virologic suppression associated with late virologic failure included older age, mostly rural clinic setting. No risk factors were identified for early virologic failure(26).

A cross –sectional Study done in Swaziland to assess factors associated with virological failure shows patients younger age less than 20 years to be associated with virological failure whereas gender was not found to be associated with virological failure(27).

A study done in Mozambique also shows younger age and illiteracy to be associated with virologic failure(28) . From study in Morocco and Kenya male sex turns out to be significant predictor of viral load un-suppression [(29)(30)]. Study in Tigray also shows male gender and age <40 years old found to be associated with virological non-suppression(14).

2.2.2. Clinical and immunologic factors

The same study in Swaziland on bivariate analysis ,clinical factor like VL >1000 at initial test, and those with CD4 count <350 cells/ml were more likely to show virologic failure at retesting ($p<0.01$ in each case) whereas Gender, WHO clinical stage, TB co-infection status, time on ART, type of facility and ART regimen were not associated with likelihood of virologic failure (27).

Tuberculosis co-infection , protease inhibitor-based regimens, and early virologic failure were found to be associated with virologic failure(26).

A study done in Mozambique in 2015 on 334 adults on first-line ART for a median of 3 years, of which 65% (214/332) had suppressed viraemia, 11% (37/332) had low-level viraemia (HIV-1 RNA 150–999 copies/mL) and 24% (81/332) had overt virological failure (HIV-1 RNA ≥ 1000 copies/mL). HIV drug resistance was detected in 89% of subjects with virological failure, but in none with low-level viraemia. ART initiation at WHO stage III/IV and low ART adherence were associated with virological failure. In addition, Longer time on ART were also associated with HIV virologic failure(28).

Patients who experienced virological failure were found to have an increased risk of clinical progression to AIDS and mortality when compared with patients with complete virological response (31). Previous studies revealed that various factors were associated with virological failure. Accordingly, baseline CD4 count((31), (32)) younger age (28), longer time on HAART((32), (28)), poor adherence to treatment (28), initial viral load >10,000copies/ml (29)and last lower CD4 count (27) were associated with virological failure.

Another case-control study done in western Kenya among 1190 HIV-infected children ≤ 15 years of age on ART, a continuous viral load monitoring was done for 12 months to determine factors associated with failure to attain virologic suppression at initial routine and subsequent VL testing among cases. Cut off point used for virologic failure was VL ≥ 1000 cps/ml. The finding shows that, being male and having baseline high viral load found out to be significant predictor of virologic failure. In Univariate analysis, Children with virologic failure at initial test were more likely to be male, have moderate or severe malnutrition, and have a history of an ART regimen change. Male children were twice as likely to have virologic failure compared to female children

Moderate or severe malnutrition was associated with virologic failure compared to those without malnutrition. Children with at least one medication change had twice the odds of virologic failure compared to those with no drug change. More than one year on ART was associated with a trend toward increased odds of failure. Roughly equal proportions of children on an NNRTI-based regimen (72%) and protease inhibitor (PI)-based regimen for first line (72%) were virologically suppressed while only 34% of those already on a PI-based second line treatment were suppressed. In the multivariable analysis of children with subsequent VL testing, children on PI-based 2nd line regimens were 10-fold more likely to achieve viral suppression than children on first-line NNRTI-based (30).

According to multicenter retrospective follow-up study conducted in northwest Ethiopia the significant predictors of failure were found to be: WHO clinical stage IV at switch, CD4 count < 100 cells/mm³ at switch and weight change (19).

A Systemic review and meta-analysis conducted in Ethiopia 2018 showed that a pooled prevalence of HIV treatment failure was 15.9% and this treatment failure is more common in Oromia regional state (18.8%) than other regional state in Ethiopia and this systemic review showed poor ART adherence, WHO clinical stage III/IV and presence of opportunistic infections are significantly associated with first line ART treatment failure(33).

Another study done in central Ethiopia to assess determinants of first line ART failure showed Lost to follow up, staying on first line ART for greater than 5 years, presence of opportunistic

infections, NVP based NNRT, late initiation of ART are determinant factors for first line ART treatment failure(34).

A retrospective followup study done in Tigray indicated Virological failure was associated with non-adherence to medications, having CD4+ T-cells count < 250 cells/ μ L and male gender. Similarly, immunological failure was associated with non-adherence, tuberculosis co-infection and Human immunodeficiency virus RNA >1000 copies/mL(14).

A retrospective cohort study done in Addis Ababa shows the predictors for antiretroviral treatment failure to be years since HIV diagnosis, weight at start, WHO stage at start, status at last visit and disclosure(13).

2.2.3. Behavioral factors

A retrospective cohort study done in Morocco including 181 patients living with HIV-1 on ART from January 1, 2007, and January 1, 2017 to see associated factors with viral load unsuppression. Five variables (male sex, initial fasting glucose >1.1 g/l, alcoholism, smoking, and initial VL >10,000 copies/ml) were significantly associated ($P < 0.05$) with unsuppressed VL. In multivariate analysis, smoking were associated independently with unsuppressed VL (29).

2.3. Conceptual framework for determinants of viral load non suppression

A conceptual framework is the totality of concepts and ideas that categorize observations and predictions. It will help researchers organize and communicate hypothesized relationships and complex phenomena by generating testable hypothesis that can be disproved later. This conceptual framework reproduced in figure 1 below specifies presumed relationship between the independent variable and the outcome variable.

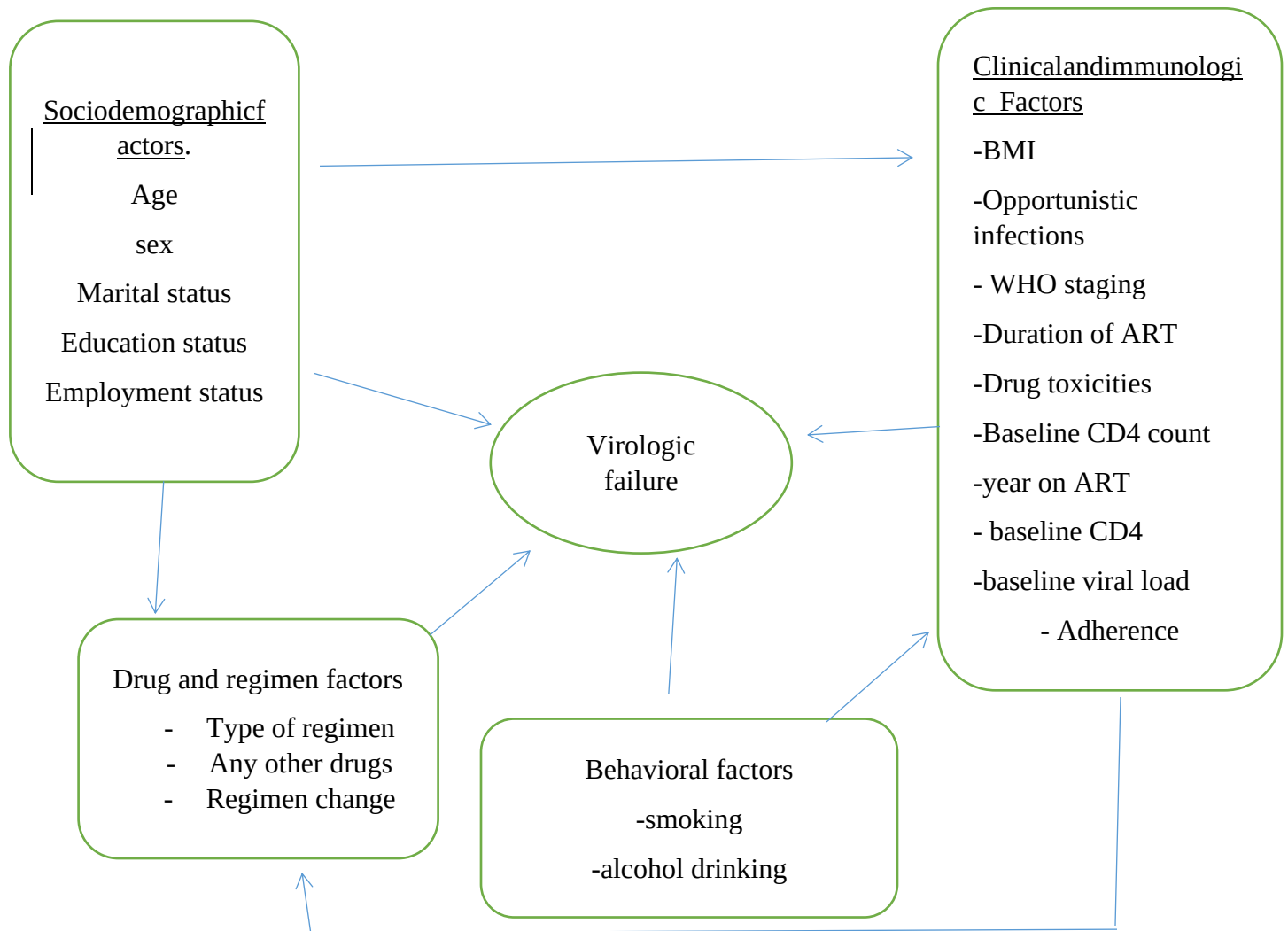


Figure 1. Conceptual framework for factors affecting virological non suppression adapted with modification from Pan Afr Med J. 2018; 29: 191(35).

3. Objectives

3.1.General objective

The aim of this study is to assess determinants of viral load non-suppression among People living with HIV AIDS on ART in Saint peter specialized hospital and Zewditu Memorial Hospital Addis Ababa, Ethiopia from December 15/2020 to February 15/ 2021.

3.2.Specific objectives

- ✓ To identify socio-demographic factors associated with virologic failure in PLWHIV AIDS on ART in Saint Peter Specialized hospital ART clinic and Zewditu memorial Hospital ART clinic from December 15/2020 to February 15/ 2021.
- ✓ To determine clinical and immunologic factors associated with virologic failure in PLWHIV AIDS on ART in Saint Peter Specialized hospital ART clinic and Zewditu memorial Hospital ART clinic from December 15/2020 to February 15/ 2021.
- ✓ To assess medication related factors associated with virologic failure in PLWHIV AIDS on ART in Saint Peter Specialized hospital ART clinic and Zewditu memorial Hospital ART clinic from December 15/2020 to February 15/ 2021.

4. Methods

4.1. Study setting and period

Saint Peter Specialized Hospital is a pioneer health facility located in Addis Ababa Gullele sub-city on entoto Road around 5km from the center of the city. The Hospital is first launched as a Sanatorium in 1953 G.C since the undergone a serious of changes and grows to be a big specialized hospital and provides clinical service for more than 5 million people per year. The chronic HIV care center was launched in 1998 and free ART started in 2006. The service is provided in the Adult, Pediatric ART, and Prevention of Mother to Child Transmission (PMTCT) clinics. Ever since the launching of the care, about 7000 HIV-infected clients were enrolled in the ART clinic. Out of these 2318 are on HAART currently. The study will be conducted from December 15/2020 to February 15/ 2021.

In addition Zewditu Hospital is also one of the largest health facilities providing a comprehensive HIV care and treatment in Ethiopia, which is found around 3km from center of the city under kirkos sub city of Addis Ababa. It was selected as the first pilot location for HIV programs and grew into a model program. In July 2003, Ethiopia's first ART program started at this health facility with support of CDC-Ethiopia and served HIV positive patients from around the country for a nominal fee. Through PEPFAR's support, the hospital began a free ART program in March 2005. Since the Hospital, one of the referral hospitals for the catchment sub city with wide geographical area, most patients have follow up in this hospital. There are more than 12000 patients enrolled to HIV care at Zewditu Memorial Hospital since 2003.

4.2.Study design

A Hospital based unmatched case control study

4.3.Populations

Cases

Source population

All HIV patients aged ≥ 15 years old attending ART clinic of SPSH and ZMH

Study population

All HIV patients aged ≥ 15 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

Source population

All HIV patients aged ≥ 15 years attending ART clinic of SPSH and ZMH whose viral load is ≤ 1000 copies /ml

Study population

All HIV patients aged ≥ 15 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

4.4.Eligibility criteria

Cases

Inclusion criteria's

Adult HIV patients aged ≥ 15 years who had At least with two viral load results, the test being done at least 3months apart and whose viral load is ≥ 1000 copies/ml

Exclusion criteria's

All patients who are lost to follow-up or transfer in and dropout with inadequate data

Controls

Inclusion criteria's

Adult HIV patients aged ≥ 15 years who had At least with two viral load results 3months apart and whose viral load is ≤ 1000 copies/ml and who have no record of viral load above 1000copies/ml

Exclusion criteria's

All patients who are lost to follow-up or transfer in with inadequate data and those who had viral load ≥ 1000 copies/ml anytime through their follow-up

4.5.Sample size determination and sampling technique

Sample size determination

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 percentage of controls being exposed 50% and from study done in Harar; variable age 45-54 with AOR=2.4 gives sample size of 221, baseline CD4<100 with AOR=2.7 gives sample size of 177 and longer duration of treatment wit AOR 3.9 gives sample size of 107 , WHO stage 3&4 with AOR 2.04 gives sample size of 318. 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(17)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 with caution to exclusion and inclusion criteria were identified first from ART unit register and smart care of both Hospital ART clinic. Screening was conducted in order to identify eligible and non-eligible study participants, as well as cases and controls. Simple random sampling was used to select study participants. Client Charts with complete and reliable information were chosen for data collection. Controls of same background and who were on follow-up during same time period as cases were selected. Precaution was taken in selection of controls to make them comparable to cases. 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 ZMH(210 total=70 cases and 140 controls).

4.6. Study variables

Outcome/ dependent variable - virologic failure

Variables of the study/explanatory variable.

Socio-demographic characteristics: – Age, Gender, Educational level, Occupation, Marital status and employment status

Clinical and immunologic factors: - Time on ART, Presence/absence of opportunistic infections, Nutritional status, Types of drugs and regimen given, HBV and HCV co-infections, Level of adherence, WHO clinical stage, Known chronic non communicable diseases, functional status, disclosure status, , baseline CD4 and baseline viral load will be the predictor variables.

Drug and Regimen related factors: - type of regimen, regimen change, reason for regimen change, any other drug co-administered,

4.7. Operational definitions

Cases: all clients on ART with viral load ≥ 1000 cps/ml

Control's: those clients who have viral copies below 1000 copies/ml

Good adherence: Drug adherence of 95% or ≤ 2 missed drug doses of 30 doses or ≤ 3 missed drug doses of 60 doses.

Poor/ Non- adherent: Drug adherence of $\leq 94\%$ or 3 or more missed drug doses of 30 doses or 4 or more of missed drug doses of 60 doses. All fair adherence and poor adherent documented in the followup constitutes poor adherence in this study

Viral non-suppression: An elevated VL RiboNuclic Acid (RNA) copies of ≥ 1000 copies/ml in plasma in a patient who has been on ART for at least six months.

Virological failure: An elevated Viral RiboNuclic Acid (RNA) copies of ≥ 1000 copies/ml in plasma on two consecutive viral load measurements in 3 months in a patient who has been on ART for at least six months.

Loss-to-follow-up (LTFU) was determined by either documentation of LTFU by the treating site, or a >12-month absence of reported clinical data prior to the date of the site's last data transfer.

4.8.Data collection methods and 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 were 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. Six health professionals were given training for 2 days. The principal investigator and one supervisor were closely monitoring the whole data collection process on a daily basis. Adherence to treatment was determined using the World Health Organization (WHO) definition in the follow-up chart.

4.9.Statistical 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). A p-value of 0.05 with 95% confidence interval was considered as statistically significant correspondingly. Bi-variate analysis were carried out for all independent variables with an outcome variable. Using variables with a *p*-value of up to 0.25, according to the bivariate analysis, a multivariable logistic regression analysis were carried out to identify the independent determinants of virological failure. 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

4.10. Data quality assurance

During preparation

Data Quality control measures were undertaken to increase the reliability of the final out comes. The questionnaire was checked by the investigator for its appropriateness such as typing error, missing questions, and inappropriateness.

During data collection

Health workers (data collectors) were given detailed explanation on the questionnaire to improve their efficiency in collecting unbiased and consistent data. In addition, the collected data were carefully checked by supervisor and principal investigator on a daily basis.

Quality of laboratory data were checked by following standard operational procedures done during sample collection, handling and transportation of those samples and also from the internal quality assurance and external quality assurance report of the ART laboratory for the investigation period.

Pretest on 5% of study participants were done at Shiromeda HC on 18 patients using the structured questionnaire to check the validity and reliability of data collection tools and necessary modifications were made based on the findings.

Data management

Every data were entered to latest version of EPI info version 7 on daily basis. Analysis was done with latest updated version of SPSS. Missed data were sorted out and excluded from the analysis.

4.11. 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. Consent were taken from medical director or ART clinic head of respective Hospital.

Each data was kept confidentially using codes and initials instead of names. Moreover, the collected data were kept safe throughout the whole process of the research work to limit data accessibility to a third party.

4.12. Plan for dissemination of results

The result of this study will be submitted to St Paul's hospital millennium medical college Department of Public Health, St Peter Specialized Hospital administration, Zewditu memorial Hospitals administration, regional health bureau, Federal Health minister and other organizations on demand. The findings of this study can be presented in the annual scientific conference of Ethiopian Public Health Association, national and Regional conferences and other similar seminars and workshops as well. Finally it will be published in reputable journals.

5. Results

5.1. Sociodemographic characteristics

A total of 350 eligible subjects were enrolled, 117 cases (those with VL $\geq$ 1000copies/ml) and 233 controls (those with VL<1000copies/ml). two hundred ten (60%) of the respondents are 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.

As displayed in Table 1 below, from total 350 study subjects, two hundred nineteen (62.6%) of the total are females while the rest 131 subjects are male which constitutes 38.4%. Coming to age category 70.9% of the cases and 54.1% of controls were in age category of 15 -39 with the rest being above or equal to 40 for both groups. Among these thirty-five (29.9%) of the cases and nineteen (8.2%) of controls are in the age group of 15-24, the study shows. 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 found out forty nine (41.9%) of cases and eighty eight (37.8%) controls were unemployed. While fairly similar number Forty nine(41.9%) of cases and one hundred nine (46.7%)of controls are employed.

Coming to education status the study classified the subject into four categories namely no formal education, primary education, secondary education and college and above. Accordingly one hundred one (86.4%) cases and one hundred seventy nine(76.8%)controls have primary and above education levels.

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

Variable	Categories	Cases	Controls
		No (%)	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 $P < 0.25$

5.2.Clinical characteristics

Body mass index eighty-two (70.1%) of cases and one hundred seventy-one (73.4%) of the controls have a normal body mass index category from 18.4 to 24.9kg/m². thirty-one (26.5%) of cases and fifty-eight (24.9%) of controls are undernourished, whereas four (3.4%) cases and four (1.7%) of the controls have a body mass index above 25kg/m². When we come to the disclosure status, one hundred one (86.3%) of cases and one hundred eighty-nine (81.1%) of the controls have disclosed their RVI status

When we come to total duration on treatment fifty-eight (49.6%) of cases and fifty-nine (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. The rest of the subjects were on treatment for less than or equal to four years as shown in the table 2 Below.

Associatively baseline opportunistic infection have been 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 while 64(54.7%) of cases and 133(57.1%) of controls have no opportunistic infection during the start of the treatment. Of the opportunistic infection tuberculosis of any type takes the greater share of the baseline OI's. twenty-eight (52.8%) of cases and 58(58.6%) of controls, of those who had OI's had some form of TB. Pneumonia and candidiasis of skin or mucosa, makes the top list when compared to the other as shown in the table.

Eleven (19.4%) of the cases and thirty-seven (15.9%) of the controls have some form of chronic diseases on top of the RVI. On the other hand, 106(90.6%) of cases and 196(84.1%) of the controls had no any type of diagnosed chronic illness until the study was conducted.

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

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%)
currentfunctional 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	<1year	4(3.4%)	5(2.2%)
	1-4years	22(18.8%)	83(35.6%)
	5-9years	33(28.2%)	86(36.9%)*
	>=10years	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 $P < 0.25$

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.

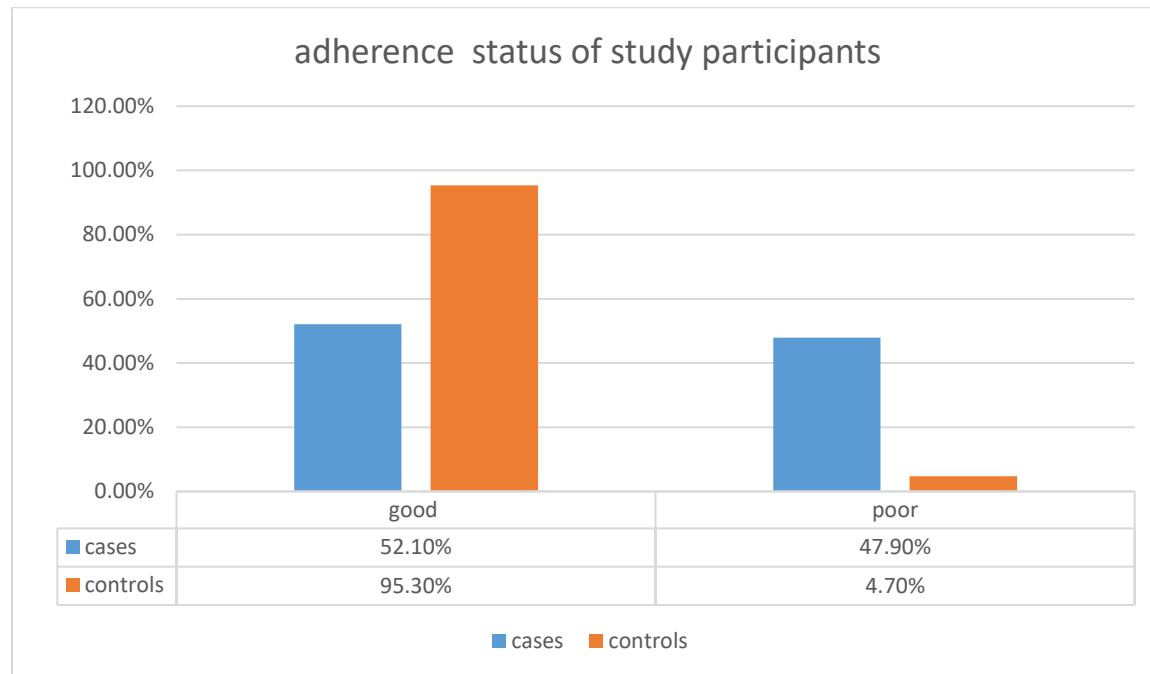


Fig 2. Adherence status and virological status of the respondents attending ART clinics in Zewditu memorial Hospital and Saint Peter Specialized Hospital Addis Ababa, Ethiopia, (n=350),2021.

5.3. Drug and regimen characteristics

When we come to regimen characteristics of the study subjects, totally 272 of the study subjects were on first line while 78 of the subjects were on 2nd line ART. Accordingly 53 (45.3%) of cases and 219(94%) of controls from the total are on the first line.

Among total 350 subjects, 327 subjects had a history of ART regimen change throughout their follow up and management. from the table 3 below, one can see that one hundred eleven (94.9%) of cases and two hundred sixteen (92.7%) of controls had history of ART regimen change throughout their follow up. The two major reason for regimen change are new drug availability throughout the course and treatment failure, even though other reason have also been mentioned.

Of the total subjects; 64(54.7%) of cases and 84 (36.1%) of controls have been taking some other medication other than the ART regimen during the study period. fifty-three (45.3%) of cases and one hundred forty-nine (63.9%) of controls were not taking any medication other than ART.

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

Variables	Categories	Cases No(%)	Controls No(%)
current regimen	1 st line	53(45.3%)	219(94%)
	2 nd line	64(54.7%)	14(6%)*
was there a change in regimen throughout management	Yes	111(94.9%)	216(92.7%)
	No	6(5.1%)	17(7.3%)
Any other drug other than 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	15(23.4%)	10(11.9%)

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

The study also analyzed reason for regimen change. The major reason is as shown below on the graph being new drug availability.

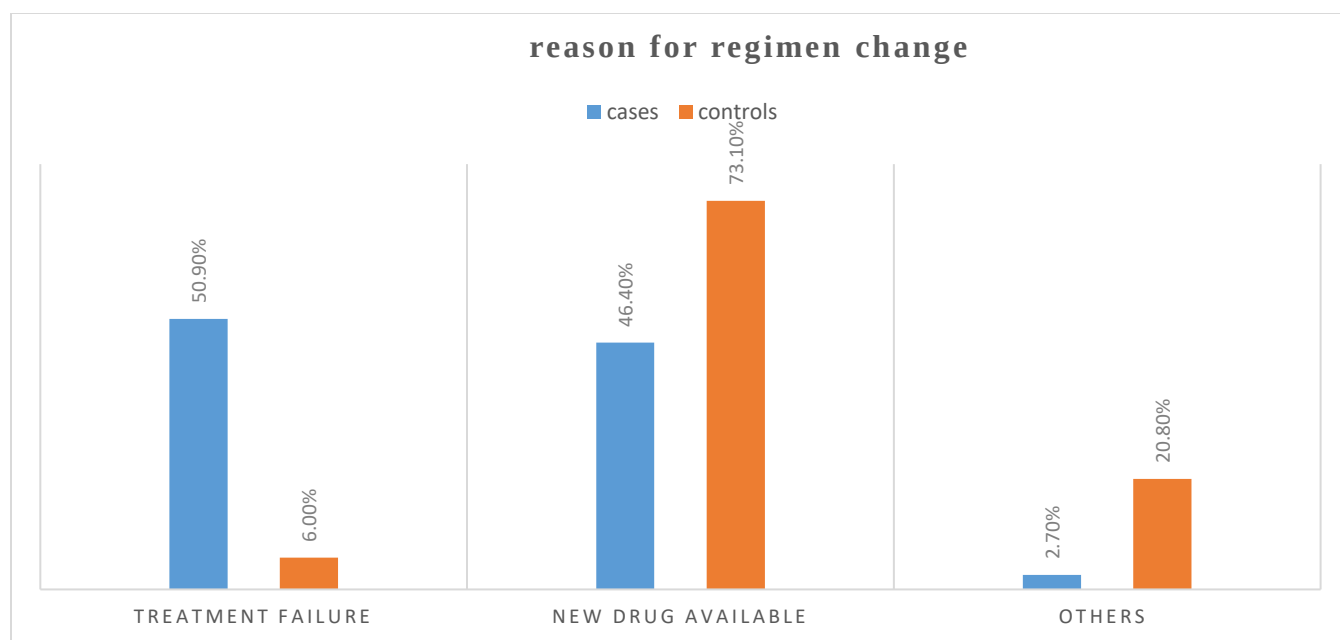


Figure 3. reason for regimen change and virologic failure in ART patients attending Saint Peter Specialized Hospital and Zewditu memorial Hospital Addis Ababa, Ethiopia, (n=350),2021

5.4. Immunological factors

When we see the baseline CD4 count of the participants, most of them fall in the category of 50-199cell/mm³ at the start of their treatment and follow up. As one can see from the table 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/mm³ at the start of the treatment which is their baseline CD4. Twenty one (17.9%) of cases and twenty nine (12.4%) of controls had a baseline CD4 count below 50/mm³. The rest of the subjects had a baseline CD4 count above or equal to 200/mm³.

In addition to that 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 1000copies/ml in their subsequent 3month follow-up.

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

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 >=1000copies/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	<1000copies/ml	39(33.3%)	12(60%)
	>=1000copies/ml	58(49.6%)	8(40%)
	undetermined	20(17.1%)	0(0.0%)

5.5. 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, $P = 0.343$) indicates well 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.

Among the sociodemographic factors analyzed by multivariable logistic regression analysis, age is the only significant independent predictor of high viral load status in this study. 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).

Among the clinical factors; disclosure status, adherence status, duration on treatment and having known chronic illness are the variables which were found to be associated significantly with having high viral load status during multivariable logistic regression analysis. The study shows that having known chronic disease and less duration on treatment is protective from risk of having high viral load while disclosing one's status and having poor adherence puts one at risk of having high viral load status. 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 is 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 don't have known chronic disease (AOR=0.14; 95%CI: 0.036-0.545; P=0.005).

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).

When we come to regimen type and characteristics, type of regimen and reason for regimen change are significant independent risk factor for having high viral load status as per the study. 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. factors independently associated with virologic failure in ART patients in Saint Peter Specialized Hospital and Zewditu Memorial Hospital Addis Ababa, Ethiopia, (n=350), 2021

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	<1year	4(3.4%)	5(2.2%)	0.814(0.208-3.183)	2.230(0.292-17.039)
	1-4years	22(18.8%)	83(35.6%)	0.270(0.149-0.488)	0.193(0.067-0.550) *
	5-9years	33(28.2%)	86(36.9%)	0.390(0.227-0.670)	0.418(0.158-1.102)

Current regimen		>=10years	58(49.6%)	59(25.3%)		
		1 st line	53(45.3%)	219(94%)	1.00	
		2 nd line	64(54.7%)	14(6%)	18.889(9.847-36.237)	7.611(1.725-33.576) *
Reason for regimen change	for	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

6. Discussion

As per the study finding being young age group, poor adherence, long duration on treatment, 2nd line regimen were the independent risk factors for virological failure. 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 (36).

However, 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, eg, the non-suppression rate of viral load in South Africa is 15%(37), mazambique 24%(28), uganda 11%(38), Cambodia 23.2%(39), and Los Angeles 27%(40). Prevalence of unsuppressed viral load in ethiopia remain very high 15.9% from meta-analysis done by Aklilu and colleagues(18). This value is very high when compared to UNAIDS 2030 95-95-95 target(41) ,but the value varies between different region. To mention some from facility based cross sectional study done in jimma, it shows high viral load status prevalence is 20.3%(42), 14.7% in Gonder(43), 11.5% in Tigray region (14), 1.3% in Addis Abeba (13), 10.7% in Bahrdar(16) and 21%in Harar(17).

Study of socio demographic risk factors of high viral load status in this study indicated, study subjects' age was significant risk factor of high viral load status in PLWHAs on ART in study areas. 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 supported by study done in Northern Ethiopia(44) Uganda(38) and Mozambique(28) which also found young age being the significant risk factor of virologic non suppression. In addition another study done in Tigray region of Ethiopia suggests age <40 as a significant predictor of high viral load status (14) 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 those adult age group(27). Similarly, a study conducted in the USA discussed that older patients were more likely to achieve viral suppression(45). A lot of factor could be the reason for this. Among these, schooling environment (for those in

schools), transition to adolescent and young adults (46), Stigma, fear of disclosure, and stress may affect younger people more than their older counterparts(47). 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 [(48), (49)].

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 in the final model (multivariable analyses).

Among the clinical factors studied in patients on ART in the study area's; disclosure status, adherence status, duration of treatment and having known chronic illness were found to be the independent predictors of high viral load status.

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 status when compared to those whose status of disclosure are unknown. In contrast to this study, facility based cohort study done in Zewditu hospital found out those that did not disclosed their RVI status are more prone to develop virologic failure(20). Another study in Addis ababa also showed that disclosure is protective of high viral load(13).

Despite the above finding possible reason could be due to stigma, loss of sexual/romantic partners, emotional harming of family/friends, shattering of privacy, physical isolation, blame, and loss of income(50) 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 HIV status disclosure is associated with clinical stage of disease. Individuals in an early clinical state (Stage I&II) of the WHO stage of disease were 78% less likely to disclose to a partner compared to those in an advanced (Stages III& IV) state of disease (51).

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; $P=0.000$). this findings coincide with study done in Africa (12), Tanzania (10), Uganda (38) Tigray(43) and Harar (17) as well as many more studies. 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(18). 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. In other words being on ART for more than 10 years is a risk factor for virologic failure. similarly, from cross-sectional study done in Felege-Hiwot Referral Hospital, Bahir Dar longer treatment duration is indicated as one of the significant risk factor for developing high viral load status and virologic failure(16). Another study done in Harar has also confirmed that longer duration of treatment is a risk factor to develop high viral load status (17) . 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 (43). In addition, as duration of treatment increases the probability of being non adherent might increase

The last clinical factor found to be associated with virological failure in this study is having a known chronic disease. The study shows having a diagnosed chronic disease is protective from developing virological failure. This finding is supported by many studies done in different time which tries 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 decrease. In other words having comorbid conditions is protective of high viral load status (52). Study done in south Africa, found no association between a detectable HIV viral load and NCD comorbidity(53).

The reason may be the enhanced care given due to the multiple comorbid condition 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.

When we come to regimen type and characteristics, type of regimen and reason for regimen change are significant independent risk factor for having high viral load status as per the study. 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. similar study done in northern Ethiopia also indicated that being on second line put patients on more risk of having high viral load (44). Another study done in Ethiopian on patient taking dolutegravir based first line management showed that Dolutegravir based regimen maintains high virological suppression (54) which supports this 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 and more drug side effect which lead to less adherence to the management.

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. no study found to support this but it could be due to patient intolerance to the new drug as well.

strength and limitation of the study

Strength:

The study design by itself being case control is a strength to identify determinant factors. The data collectors were blinded to the study group. were not told which group is case or which group are controls.

Limitation: The study used a secondary data, some information which might be useful were not assessed, for example information like income, behavioral factors were not assessed.

7. Conclusion and recommendation

Conclusion: - In summary, this study identified some of the 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 -suppression. 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 the most impact on patients lives and as well as ART service in general.

Recommendation :-

- Health professionals should give due attention in counselling and management of young age group which are on ART to modifying their risky behavior which might be the reason for their poor adherence and subsequent virologic failure
- All ART clinic management should give high priority to those who have poor adherence and they should be put on EAC. Their reason should be sorted out and tried to be solved as possible
- MOH, RHB and all other stakeholder should plan for how to improve counselling sessions, patient behavioral management sessions and patient support mechanism specially for those who have been on treatment for long time.
- Reason for treatment failure should be sorted out and managed before switching the regimen, by anybody concerned
- Further research should be conducted to find a way to modify those risk factors which are modifiable

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Annexes

Annex: 1 English version of the questionnaire

Assessment of determinant of virologic non suppression among clients in St. Peter specialized hospital and Zewditu Memorial Hospital, Addis Ababa, Ethiopia – a hospital based unmatched case control study

Questionnaire

	Section 1: Socio-demographic characteristics of the woman	
S.no	Question	answers
1.1.	sex	a. Male b. Female
1.2.	What is your age in years?	_____

1.3	Current place of residence (from 2 ^o dat?)	1.urban 2. rural
1.4	Marital status	1.married 2.un-married 3.widowed 4.divorced 5. separated
1.5.	What is your employment status?	1. Unemployed 2. Employed 3. Self employed 4. House wife
1.6.	Educational level?	1.no formal education 2. can write and read 3.primary education 4.secondary education 5.college or above
Section two. Clinical factors.		
2.1	Base line body mass index (BMI)	1. <18.5kg/m ² 2. 18.5-24.9kg/m ² 3. 25-29.9kg/m ² 4. ≥30kg/m ²
2.2	Functional status	1. Working 2. Ambulatory 3. Bed ridden
2.3	Disclosure status	1. Disclosed 2. Not disclosed 3. unknown
2.4	Date treatment started	_____

2.5	How long since treatment started	_____
2.6	Adherence to treatment	1. Good 2. Fair 3. poor
2.7	Current WHO stage	1. I 2. II 3. III 4. IV
2.8	Opportunistic infection	1. Yes 2. no
2.9	If answer to question 2.8 is yes, what is it?	1. TB 2. Toxoplasmosis 3. PCP 4. HBV/HCV 5. Cryptococcal meningitis 6. Kaposi sarcoma 7. Other_____
2.10	current regimen	1. ZDV/3TC/NVP 2. ZDV/3TC/DTG 3. TDF/3TC/NVP 4. TDF/3TC/EFV 5. TDFF/3TC/DTG
2.11	Is there change in you regimen throughout the course	1. Yes 2. No
2.12	If there was a change what was the reason	1. Drug side effect/toxicity 2. Treatment failure 3. Drug stock out 4. Viral load>1000 5. Other
2.13	What is your smoking history?	1. Never smoked 2. Quit smoking 3. Currently smoking
2.14	Do you drink alcohol	1. Yes 2. No
2.15	Any known chronic illness	1. Yes 2. No

2.16	Any other medication being administered other than ART	1. Yes 2. No
2.17	If answer to Q2.17 is yes, how many types are you taking other than ART	1. 1-2 2. 3-4 3. 5 and above
	Section three Immunological factors	
3.1	Base line CD4	1. ≤ 50 2. 50-200 3. 200-500 4. ≥ 500
3.2	Baseline viral load	A if determined _____ B. not determined
3.3	Is there viral load above 1000cps/ml any time though your follow-up?	1. Yes 2. No
3.4	If answer to 3.3 is yes, what was your result in subsequent 3month follow-up?	1. ≥ 1000 copies/ml 2. < 1000 cps 3. Not determined