COLLEGE OF HEALTH SCIENCES SCHOOL OF PUBLIC HEALTH

TIME TO VIRAL LOAD SUPPRESSION AND ITS PREDICTORS AMONG ADULT HIV PATIENTS WITH HIGH VIRAL LOAD ON ANTI RETROVIRAL TREATMENT IN SELECTED HOSPITALS OF SOUTHERN ETHIOPIA: A RETROSPECTIVE COHORT STUDY.

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HAWASSA, ETHIOPIA

Time to viral load suppression and its predictors among adult HIV patients with high viral load on anti -retroviral treatment in selected hospitals of southern Ethiopia: A retrospective cohort study

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A Thesis submitted to Hawassa University School of Public Health, in partial fulfillment of the requirements for the degree of master in public health

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Declaration

I hereby declare that this MPH thesis is my original work and has not been presented for a degree in any other university and all sources of material used for this thesis have been duly acknowledged.

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Acronyms or Abbreviations

3TC	Lamivudine
ABC	Abacavir
AHR	Adjusted Hazard Ratio
AOR	Adjusted Odd Ratio
ARR	Adjusted Relative Risk
AIDS	Acquired Immune Deficiency Syndrome
ART	Anti-Retroviral Treatment
AZT	Zidovudine
ARV	Anti Retro viral
BMI	Body Mass Index
CD4	Cluster of Differentiation 4
CI	Confidence Interval
DTG	Dolutegravir
EAC	Enhancement Adherence Counseling
EFV	Efaviren
HIV	Human Immunodeficiency Virus
MPH	Master of Public Health
NVP	Nevirapine
OI	Opportunistic Infection
OR	Odd Ratio
PI	Protease Inhibitor
PLHIV	People Living With HIV
RNA	Ribonucleic Acid
TB	Tuberculosis
TDF	Tenofovir
UNAIDS	United Nations Programme on HIV/AIDS
VL	Viral Load
WHO	World Health Organization

Abstract

Background: More than 1000 copies of the HIV per milliliter is strongly associated with poorer survival of patients and increased new transmissions of virus. Determining time to viral load suppression and its predictor among HIV patient was crucial to evaluate the implementation of routine viral load monitoring, treatment response and progression toward national target.

Objective: To determine time to viral load suppression and it's predictors among adult HIV patients with high viral load on anti- retroviral treatment in selected hospitals of southern Ethiopia.

Method: A retrospective cohort study was conducted among 344 adult HIV patients initiated to ART from January 01, 2016 to December 31, 2022 on first line treatment regimen. A simple random sampling technique was used to select study participant. Data were collected by Kobo Toolbox and extracted to SPSS for data analysis. Kaplan-Meier was used to estimate time to viral suppression. Cox-proportional hazard model was used to determine independent predictors of viral load suppression. Adjusted hazard rate with 95% CI reported and p-values <0.05 was used to declare statistical significance in multivariable analysis.

Results: A total of 344 HIV patient records were reviewed. In this study the overall median time to viral suppression was 5 months. The incidence rate of viral load suppression was 15.3 per 100 person-months. The study found that factors such as no opportunistic infection (AHR: 1.44; 95% CI: 1.06, 1.96), no substance use (AHR: 1.54; 95% CI: 1.19, 1.99) and baseline CD4 cell counts 200-350cell/mm3 (AHR: 1.75; 95% CI: 1.24, 2.45), and >350cell/mm3 (AHR: 1.53; 95% CI: 1.02, 2.28) were associated with higher chance of viral load suppression. Being on ART drug regimen TDF+3TC+NVP (AHR: 0.21; 95% CI: 0.07, 0.68), and AZT-3TC-EFV(AHR: 0.50; 95% CI: 0.26, 0.96) and ART duration 13-24 months (AHR: 0.72; 95% CI: 0.53, 0.98), 25-59 months (AHR: 0.68; 95% CI: 0.50, 0.93) and above 60 months (AHR: 0.26; 95% CI: 0.12, 0.58), were associated with less chance of viral load suppression at multivariate analysis.

Conclusion: The median time to viral suppression was 5 months. Opportunistic infection, baseline CD4 counts, ART dugs regimen, duration on ART and substance use were independent predictors of time to high viral load suppression after controlling for others factors.

Prioritizing interventions targeting opportunistic infections and substance use cessation, initiate to DTG contain ART drug regimens could improve viral load suppression and patient outcomes.

Keyword: Anti-Retroviral Treatment, High viral load, Predictors of high viral load suppression.

1. Introduction

1.1. Background

The Human Immunodeficiency Virus (HIV) targets the immune system of infected people and weakens their defensive ability against infection. The immune cells of infected individual could not perform their basic function of defense against antibody if not treated. The major methods to acquire HIV infection from infected individuals through exchange of body fluids during sexual intercourse, commonly use sharp materials, mother to child during pregnancy, delivery and breast feeding (1)(2).

Early and properly untreated individual can develop Acquired Immunodeficiency Syndrome (AIDS) which is the complicated and life threat stage of HIV infection (1). To manage HIV/AIDS infection all Peoples living with HIV (PLHIV) have immediately initiate to antiretroviral (ARV) drugs treatment. PLHIV does not cure from HIV infection whenever initiate to antiretroviral therapy (ART) but ART could decreases viral replication that important to strength and recover immune systems of individuals to capacitate defensive against opportunistic infection (3).

According to the national guideline, newly HIV diagnosed patients have to start with fixed dose of first line regimens which take once-daily dose combinations of two Nucleoside Reverse Transcriptase Inhibitors (tenofovir (TDF)/emtricitabine (FTC) or abacavir (ABC)/lamivudine (3TC)) or (TDF or FTC +3TC) as build block and one Non-Nucleoside Reverse Transcriptase Inhibitor (NNRT) efavirenz (EFV) or integrase inhibitor, Delotagravir (DTG) are the preferred and are AZT + 3TC + EFV, AZT + 3TC + NVP and TDF + 3TC + NVP alternative choices of first regimens with less toxic, simple, more effective and convenient for adults regimes (2–4).
Viral Load (VL) is the concentration RNA of HIV in the patient blood and it is the golden standard to monitoring the treatment response in HIV-positive patients. It is measure the amount of HIV RNA copies per one milliliter blood (3).

After three years of World Health Organization (WHO) in 2013 introduce the routine VL testing, the Federal Ministry of Health, in 2016 adopt and recommended it for all HIV positive patients on ART have to receive routine VL at 6 months after initiate to ART, at 12 months and then every 12 months. The goal of HIV treatment is to achieve VL suppression in HIV patients in order to achieve better clinical outcomes, lower risk of HIV transmission, and to reduce persistent viral replication that can lead to resistance to one or more ARVs (2–5).

In most patients taking ART, their VL should be ≤1000 copies/ml after 6 months of treatment and VL suppression is defined for HIV patients with VL (≤1000 copies/ ml) after 12 months on ART. When a client is found to have a viral load of >1000copies/ml on routine or need-based viral load test, classify as high (unsuppressed) VL are link to EAC for 3-6 months to address adherence related issues. After 3month repeat VL test will be recommended for individual with good adherence, but for those patients with adherence barriers, repeat VL test is advisable to extend for 6 months. HIV client with repeat VL test result (< 1000 copies/ml of blood) is virally suppressed and continues on the same ART regimen. On the other hand, patient with repeat VL test result is high (>1000 copies/ml) with good adherence to therapy is defined as unsuppressed VL and switch to second line ART drugs (3,5).

The Global health sector develops strategy that all countries are responsible to reach the UNAIDS fast track to achieve the target so called 95-95-95 by 2030 to ending HIV/AIDS epidemic. This target means at end of 2030, the first 95% of all people living with HIV will know their HIV status, the second 95% of all people diagnosis to HIV infection will link to ART, and third 95% of all people receiving ART will have viral suppression (4,5).

1.2. Problem statement

HIV continues to be a major global public health issue. According to WHO reports in 2021 globally peoples around 38.4 million are HIV careers, 1.5 million are newly acquired HIV, 665,000 are died with HIV and its related infection and 28.7 million are linked to ART. Among of the most affected regions the sub Saharan Africa shared around two-third of global HIV cases but the more worst issue is one in every 25 adult of reproductive age group are living with HIV (1,6).

From sub Saharan Africa, Ethiopia is one among 30 countries that contributes 89% of all new HIV infection together to worldwide (7). And around 718,000 people are living with HIV/AIDS, and 20,000 people die annually as UNAID report in 2018 (3). The adult HIV prevalence in Ethiopia is 0.9%, with varying burdens by sex, age, and other demographic characteristics, across sub-regions and population groups (8,9).

Viral load suppression is the measures of treatment response and the third target of UNAIDS fast-track to ending HIV epidemic by 2030. Despite progression global uptake, viral load tests in last five years with approximately 20 million test are performed within low and middle income countries but still viral load suppression is low with only 59% of patient virally suppressed and huge variation of VL suppression across countries when compare to third 90% of 2020 target (9) According to study of Ethiopia progression toward 2020 fast-track reveals the incidence of HIV decreased by 77% in under five age while increased by 12% in adult 15-49 age in 2017 from 2010 baseline (9). Evidence from southwestern Ethiopia illustrate among HIV patient 20.3% of them have VL >1,000 copies/mL after more than 6months enrolled to ART (10). Similarly the report in Ethiopia 83.3% of VL suppression is observed at first test with around 17% of adult need repeat VL test result after 3 to 6 months (11).

According to evidence of systematic and meta-analysis mostly from African countries states only 53% of HIV patients VL re-suppressed after EAC service (12). Although the studies from different regions of Ethiopia country shows the incidence of VL re suppression among high VL adult HIV patients; from public hospitals of North Wollo zone, West Gojjam Zone and public

hospitals of Hawassa city are 66.4%, 51.4% and 40.9% respectively (13–15) Collectively, the evidence suggest that there are variation in Ethiopia regions that will need attention to reach WHO target70% among HIV patients with initial VL >1000copies/ml have to re-suppressed after 3-6months (12).

Most of studies conducted on HIV patient with high viral load are focused on incidence and predictors of VL suppression. But there are no studies to assess time to viral suppression after high VL detected in adult HIV patients. Different studies are indirectly tries to illustrate the matter of time during EAC service. According the studies from public hospitals of Noth wollo zone the median time to start and completes EAC is between 4-8weeks and 8-25weeks, respectively (13). Another study from West Gojjam Zone reveals the median time to complete EAC session and take repeat VL test result after complete EAC session is between 10-33weeks and 0-6weeks respectively (14).

Unclear contextualized average of times to VL suppression in adult HIV patients primary increases the threat of morbidity and mortality, increase burden on Health facility, risk to HIV transmission between sexual partners, high potential risk to treatment failure and incorrect switching time to second line regimens. Secondary causes low productivity that increases economic dependence in country and family level and challenges the transition to elimination of HIV by 2030s (13,14,16).

Different studies are reveals different predictors of VL suppression after high viral load diagnosed, Age, Sex, Occupations, Marital status, Residence, Opportunistic infection, Nutritional status, duration on ART, WHO clinical stages, CD4 count, initial VL, prophylaxis against opportunistic infections, adherence level and complete EAC session are reported to have association but with not statistically similar in all studies (11,13–21). Some important variables have potential association with VL suppression such as the newly introduced treatment drug, Social problem, Mental and Behaviors were not considered in previous similar studies design (22–26).

1.3. Significance of the Problem

Ethiopia is the one among a few countries with double burden of HIV infection and poverty. To light this burden continuously and systematically monitoring and evaluation of patient progression and treatment outcome are important for both individual and country. Specially focus to quality of Service with routine VL monitoring, and adequate treatment, are the last opportunistic window in improving overall clinical outcomes and drug resistance in HIV patients with high viral load.

Studies regarding, time to VL suppression after first high viral load detection are limit in Ethiopia, particularly in southern part of country in context of routine VL monitoring for adult HIV patients. This study is design to determine actual time to VL suppression, and predictors of highVL suppression among adult HIV patient with high viral load in Dilla and Bule Hora university referral hospital. The finding of this study was help Ethiopian Ministry of Health, both study areas, and other stakeholders to assess the implementation status of the national guidelines mainly focus on timeliness of routine viral load monitoring and other service provided to improve the quality life of HIV patient's.

2. Literature review

2.1. Overview of high viral load suppression

For first time elevated viral load above 1000copies/ml in HIV patient on first line ART drug regimens should be suppressed before decelerate treatment failure. Different studies show the variation in proportion of high viral load suppression after patient supported by EAC program. Based on used studies references WHO consolidated guideline on the use of ART drugs for treatment and preventing HIV infection updated in 2021 reveals proportion of viral load suppression is vary from 70% to 87%. This variation is explained by duration for test and used ART drugs (4).

According to retrospective study from India shows among patient initiated to EAC session 88% of them experienced viral load suppression (27). The randomized control trial study from Nigeria reveals around 90% of first high viral load HIV patient observed viral suppression in study participants (28).

Retrospective study conduct for 669 high VL patients that linked to EAC service in South Western Ethiopia, show viral load suppression (≤1,000 copies/mL) is observed in 79.7% of HIV patients but 20.3% of them have unsuppressed viral loads (>1,000 copies/mL) after ≥6 months' ARV therapy (10).

Three retrospective cohort studies in Ethiopia, on HIV patients with a first elevated VL (>1000 copies/ml) are shows the difference in proportion of viral load suppression after six months in repeat testing result with 66.4%. 64% and 40.9% Amhara, Oromia and Sidama region respectively (13,15,29).

2.2. Time of high viral load suppression.

Survival time of high viral load in HIV patient is minimized by early initiation to ART. Many countries across a world accept the WHO recommendation that the survival time of high viral load in HIV patients is between 3-6moths if correctly address the adherence barriers of drugs (4).

But the evidence of studies from different countries illustrate the variation of survival time with high VL with depend on duration of follow up and quality of service. Among that the Zimbabwe retrospective cohort study on 646 patient with first high VL and reveals after followed for three month from total 444 patients receive second VL test result but only 201 patients are free survival time from high VL with 3months (20). Other retrospective study in Kenya states that the median time to unsuppressed VL in 58% of first high VL HIV patient is 6months (30).

Although as retrospective study from West Gojjam zone of Ethiopian country show, among adult HIV patients with high VL, the median time of follow up is 5month with minimum three month and maximum 6month. And also the incidence of viral suppression at five months of EAC session of HIV patients are 11.53per 100 person-months respectively (13). Similarly studies from Nigist Eleni Mohammed memorial comprehensive specialized Hospitals southern Ethiopia indicate median time to viral suppression was 9months (31). Others study conducted in three hospitals of Amhara region of northern Ethiopia on adult HIV patients for more than 9month on ART to analysis the survival time to unsuppressed VL in HIV patient indicate the cumulative probability of free survival time is decline while the duration patients on ART is rise (32).

2.3. Predictors for high viral load suppression

2.3.1. Socio - Demographic predictors of time to viral Load suppression

As different studies detected the socio-demographic variables are significant predictors of VL suppression with different statistical expression due to study methods and sample size used. Viral suppression different between sex of socio-demographic variables in different studies where are districts of south-central Uganda men are twice than women associated with high persistent viral load (21). Contrarily two studies from north Ethiopia illustrate females are 1.2 and 1.50 times more likely to have VL suppression than male participants in North wollo and West Gojjam zone of Ethiopia respectively (13,14). Marital status also significant in viral suppression as studies from South western Ethiopia and East shawa of Oromia region (10,30).

2.3.2. Clinical related predictors

Different studies on predictors of VL suppression mainly focus on clinical characters of patients. Among those the Rwanda study show some variables significantly associated with unsuppressed HIV viral load such as history of opportunistic disease since the HIV positivity (33).

Retrospective study from the North of Ethiopia reveals the study participants with the CD4 count greater than or equal to 350 cells/mm3 are estimated to have 1.98 times higher hazard of viral suppression compared to those who have CD4 count less than 200 mm3, when all other variables held constant (13). On top of that study measure time to failure of VL suppression shows the significance of baseline CD4 count <200cells/mm3 ($p<0.0004$) (34). Another study illustrate unsuppressed viral load is 2.76 times as likely among those with baseline CD4 ≤100 cells/ml (10).

According to retrospective cohort studies in Northern of Ethiopia on 235 adult HIV patients with high viral load reveals frequency of VL suppression is depend on numbers of base line viral loads, as patient categorized in 5001-10,000 copies/ml are less than 7% of probability to their VL suppression than those who have 1000–5000 copies/ml (13). Although similar study from northern Ethiopia strength the previous evidence with probability of VL suppression is 56% lower in patients with base line VL greater than 10.000 those with 1000–5000 copies/ml (14).

Patients with WHO clinical stage III and IV are 4.47 time hazard to unsuppressed VL than stage I and II patients as evidence North West Ethiopia (32). As study conducted in South Africa indicates, among adult HIV patient with elevated VL and no OI are 1.85 times to VL suppression than those have OI. Other significant predictors in this study is patients with history of hospitalized are lower probability of viral load suppression than not hospitalized (35).

Study conducted in Southern Ethiopia reveals there is different time of viral suppression within predictors as, shorter time for those CD4 count greater than 200cell/mm3 as compared with those less than 200cell/mm3, WHO clinical stage I and II with stage II and IV stage and no opportunistic infection with had opportunistic infection respectively after used Kaplan-Meier analysis (31).

2.3.3. Anti-Retro viral and other preventive Therapy related predictors

A study from Oxford University after followed for 18447 persons-year, the hazard time to viral suppression in DTG based regimens when compared with others (36).

Retrospective cohort studies in North of Ethiopia shows DTG-based regimens have higher probability to suppress VL when compared with study participant received EFV-based regimens (14). And another study also states as, after DTG introduced the overall, VL suppression increased from 81% to 92% (11). Although other study from Northern Ethiopia shows as observed variation of survival experience between patient due to receiving EFV and NVP regimens and patient with adherence more than in those who are in poor adherences (33) and other study in Southern Ethiopia reveals late VL suppression is observed in participants received NVP-based regimens than those on PI-based regimen and also those received an EFV-based regimen have a lower probability of VL suppression than those on a PI-based regimen (15).

Other variables related to ARVS are described in different studies as follows. retrospective study conducted in Rwanda show HIV patients with fair and poor quality of adherence are significantly associated with unsuppressed HIV viral load (21). Drug side effect have 2.47 times hazard to fail VL suppression in patients on first line regimens when others variables controlled in retrospective study of Northern Ethiopia (33). Having history of drug substitution, time since HIV diagnosis, and duration on ART, is significantly associated with failure of VL suppression as studied in Arba Minch hospital of Ethiopia in 2018 (34).

2.3.4. Psychosocial problem and others service related predictors

Different studies are states the impact of EAC service in VL suppression after high viral load >1000 copies/ml is detected in HIV patient. As evidence collected by Systematic review and Meta-analysis conducted in 2019 on 58 studies from different countries are indicates patients with an initial high viral load are re-suppressed in studies focused to EAC with 53% as compared to not describe EAC with 43.3% (12).

As study done to know the effect of substance use on sustained viral suppression among study participants illustrated participant used substance had in low viral suppression when compared to those who reported not use substance (37). Similarly study from Canada shows the rate of viral suppression between study participants who are alcohol drinkers 1.97 times higher than not drinkers (38).

According to retrospective study conducted in India, among high viral load patient linked to EAC only 28% of patients achieve VL suppression after 8%, 48% and 44% have attend one, two and above three EAC session respectively (27). A study conduct in Zimbabwe describe patient attend 3 sessions of EAC have higher probability than non-attend to achieve VL suppression (20). Studies from Cameroon and Guatemala illustrate among HIV patients VL suppression with 54% and 74% in Cameroon, while 74% and 89% in Guatemala at 12months and 12-24months on ART respectively after assessed the effect of ART duration on VL suppression (24).

Bidirectional relationship of mental health and HIV are discussed in different literatures, as majority of HIV patients are also have the problem of psychosocial and of mental health like depression, anxiety, alcohol and drug dependence (39). The results of study in South Western Uganda on adolescent living with HIV infection that have no social problem and diagnose with no malnutrition are significantly associated with viral load suppression. But HIV career discloser have no significant association in VL suppression (40).

Study conducted in South western Ethiopia to identify none virological predictors of VL suppression in HIV patient with high VL reveals those patient with moderate malnutrition and severe malnutrition are 2/9 and 4.4 times risk to unsuppressed VL than normal (10). Similar evidence from other study of Southern Ethiopia shows there are significant differences in survival times of failure to VL suppression is high in the categories of substance use (34) .

Conceptual Framework

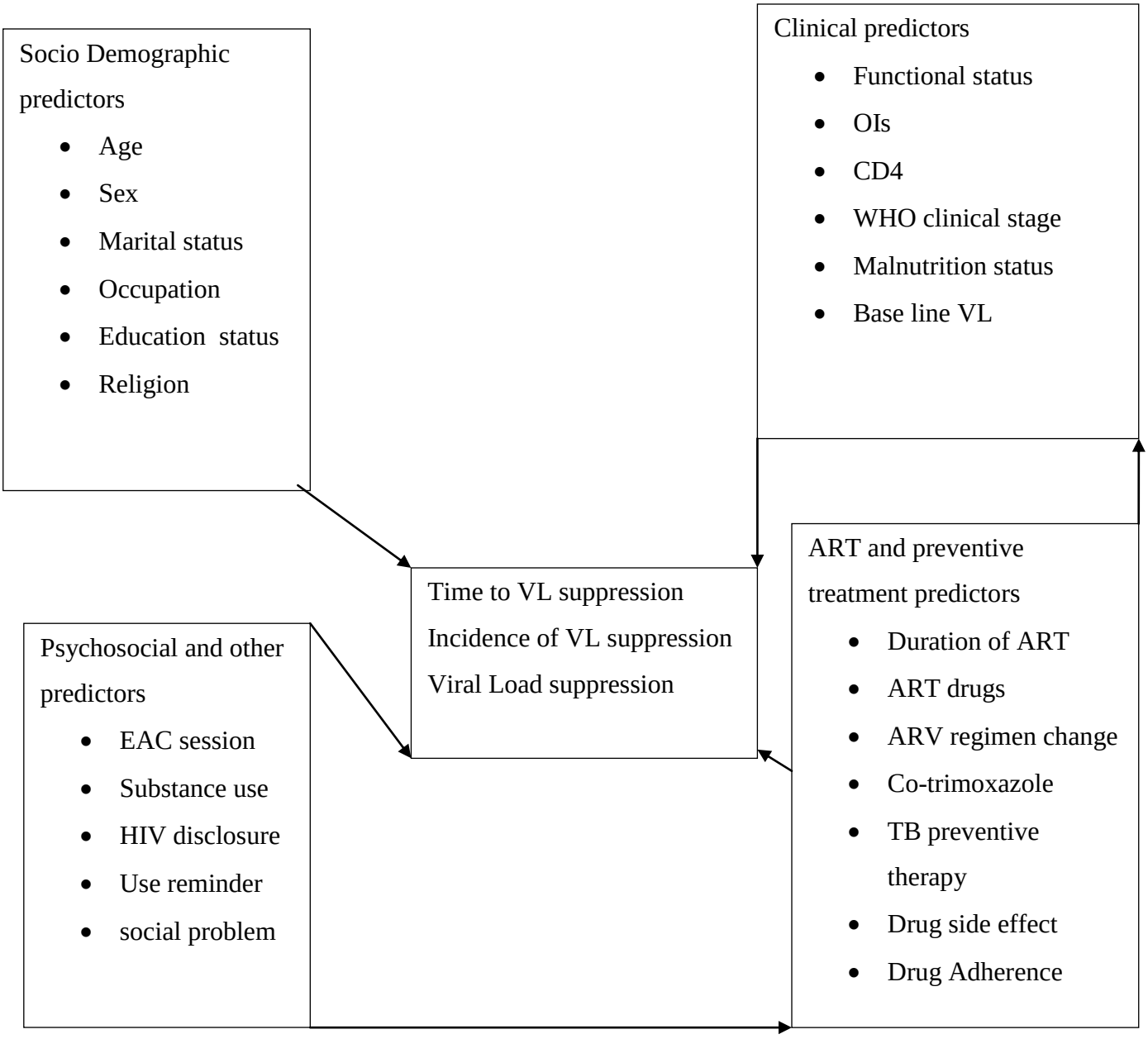

Figure 1: Conceptual Frame work of time to Viral Load Suppression and its Predictors among adult HIV patient in selected hospitals of southern Ethiopia in 2016-2022 (3,5,13,15).

3. Objectives

3.1. General objective

To determine time to viral load suppression and it's predictors among adult HIV patients with high viral load on anti- retroviral treatment in selected hospitals of southern Ethiopia in 2016-2022.

3.2. Specific objective

1. To determine time to viral load suppression among adult HIV patients with high viral load on anti- retroviral treatment in selected hospitals of southern Ethiopia.
2. To determine incidence of viral load suppression among adult HIV patients with high viral load on anti- retroviral treatment in selected hospitals of southern Ethiopia
3. To identify factors associated with viral load suppression among adult HIV patients with high viral load on anti-retroviral treatment in selected hospitals of southern Ethiopia.

4. Method and materials

4.1. Study area

This study was conducted in two selected University Hospital in two regional states at southern Ethiopia. The hospitals were Bule Hora Hospital in West Guji Zone of Oromia Regional State and Dilla Hospital in Gedeo Zone of South Ethiopia Regional State. Both hospitals are located at south of Addis Ababa the capital city of Ethiopian country on the pave of Addis Ababa–Moyale highway.

The Dilla Hospital is found in Dilla Town, which is capital town of Gedeo Zone administration and located at distance of 361 kilometers to Addis Ababa. It serves for approximately two million people and as referral center for patients referred from health centers, district hospitals and other private health facilities in Gedeo Zone and others from neighboring Sidama and Oromia regions.

The Bule Hora University Referral Hospital is situated in the capital town of Bule Hora, in the West Guji Zone of the Oromia Region, 103 kilometres from Dilla town and 464 kilometres from Addis Ababa. Initially the hospital established as a primary hospital in 1998, it has evolved into a general hospital in 2015 and a teaching hospital in May 2022. It serves 1.5 million people in total for the residents of the West Guji Zone and the adjacent areas. Since 2005, the hospital has provided ART services to patients diagnosed with HIV through various counseling and testing protocols, ensuring their registration and data transfer to an electronic database.

4.2. Study design and period

A retrospective cohort study was conducted to estimate time to high viral load suppression and its determinants in adult HIV patients. In this study, patients who commenced antiretroviral therapy (ART) between January 01, 2016, and December 31, 2022, and exhibited a viral load (VL) test result exceeding 1000 copies/ml after 6 months on ART were considered as exposed.

4.3. Population

4.3.1. Source population

All PLHIV who are on the first-line regimen and had viral load greater than 1000copies/ml after 6 months on ART after newly initiated to ART from January 01, 2016 to December 31, 2022 at Bule Hora and Dilla University referral hospitals of southern Ethiopia.

4.3.2. Study population

Randomly select PLHIV who are on the first-line regimen and have experience of viral loads greater than 1000copies/ml among newly initiated to ART from January 01, 2016 to December 31, 2022 at Bule Hora and Dilla University referral hospitals of southern Ethiopia.

4.4. Inclusion and Exclusion criteria

4.4.1. Inclusion Criteria

HIV diagnosed patients who had documented viral load results greater than 1000 copies/ml after 6 months on ART, and age greater than 15years old.

4.4.2. Exclusion Criteria

HIV Patients who were pregnant and lactating women and with incomplete data were excluded from the studies.

4.5. Sample Size Determination

For objective one: Sample size calculated with the assumption of type one error 5%, power 80% median time to viral load suppression among exposed and non-exposed group (opportunistic infection) 5months and incidence rate of viral load suppression 11.17/person months from previous study (13). By using log rank formula with cox-proportional hazard assumption (41).
The maximum sample size required for each group after adding of 10% for incomplete records the sample size is 133 for each group. The total sample size for first objective is 266.
For objective Three: Sample size for predictors of viral load suppression is calculated using two sample proportion formulas by using Open Epi online software.

$$N1 = [Z\alpha/2\sqrt{(r+1)\,p\,q} + Z\beta 1-\sqrt{rpq1+p2\,q2}\,]2, \quad n2=rXn1$$

$$r(p1-p2)2$$

Where:

N1= number of Exposure

N2= number of none exposure

r=the ratio of exposure to none exposure

P1= proportion of VL in exposure

$p = \frac{p1+r\,X\,p2}{r+1}$; $q=1-p$

P2= proportion of non-exposed group

α =Type one error (0.05)

Zα /2= Critical value at 95 % level of significance

Zβ1-= standard normal distribution value corresponding to power

To determine the sample size, a retrospective cohort study conducted at West Gojjam and North Wollo Zone hospitals, Northern Ethiopia is considered.

(1)Table 1. Samples size calculation for time to Viral Load Suppression and its Predictors among adult HIV patient in southern Ethiopia in 2016-2022.

Predictors considered	statistics	Sample size plus 10%	reference
CD4	95% CI= (1.12–3.51) AHR =1.98 Ratio =1 Power = 80% Proportion of unexposed with outcome =16.6%	244+24=268	(13)
Gender	95% CI= (1.05–2.15) AHR =1.50 Ratio =1 Power = 80% Proportion of unexposed with outcome =32.4%	312+32=344	(13)
Duration on ART	95% CI= (0.130–0.949) AHR =0.35 Ratio =1 Power = 80% Proportion of unexposed with outcome =26.9%	172+17=189	(14)

So the final sample size is 344 with $n_1=n_2=$ 172

4.6. Sampling technique and sampling procedure

Bule hora and Dilla University referral hospital were purposely selected for the study in order to get adequate number of sample size, optimal time of routine viral load. A total 2147 (1004 from Dilla Hospital and 1143 from Bule Hora Hospital) patients were newly initiated to ART clinic from January 01, 2016 to December 31, 2022. Of 2147 patients 516 (246 from Dilla and 270 from Bule Hora Hospitals) were diagnosed with having high viral load. Out of 246 from Dilla Hospital, 176 patients fulfilled inclusion criteria. Similarly of 270 from Bule Hora Hospitals, 193 patients were met inclusion criteria. Proportional allocation was used to determine total sample size between both studies area. For patient fulfill inclusion criteria simple random sampling technique based on unique Identification numbers was separately used to select total 344 (164 from Dilla Hospital and 180 from Bule Hora Hospital) sample.

4.7. Variables

4.7.1. Dependent variables

Viral load suppression (Yes/No)

Time to viral load suppression, (≤ 1000 copies of viral RNA/ml of blood plasma/dried)

Incidence rate of viral load suppression

4.7.2. Independent variables

Explanatory variables are:

Socio demographic variables: Sex, age, marital status, religions, occupation, educational status.

Clinical related variables: Baseline CD4 count, baseline viral load, WHO clinical stage, body mass index (BMI), opportunistic infections, and functional status,

ART and treatment related variables: Duration on ART, type of first-line ART regiment, ART treatment change, drug side effect, Cotrimoxazole-preventive therapy status, Isoniazid-preventive therapy, and ART drug adherence.

Psychosocial and others related variables: Reminder to take drug, disclosure status, substance use, social problem, and attended EAC session.

4.8. Data Collection Technique

Data collection tool was prepared by principal investor based on recommendation of WHO, National guideline and previous study after compare with exist data capture form and register of follow up. The secondary data were collected by Kobo Toolbox. Kobo Toolbox was used to develop data extraction format on a web interface, deployed online created form to mobile and collect the data. Socio-demographic, clinical, ART and treatment, and psychosocial and others data were collected from patient follow up card, EAC sheet, patients VL registration, and electronic data base. Data which are most nearest to the exposure date of high VL are considered as baseline. Follow up data are those collected, during high VL patient on first line regimens treatment within follow up period.

4.9. Data quality and management

The data collection tool (extract format form) was prepared in English language and developed on kobo Toolbox application. Pre-test was conducted on 5% of randomly selected study participants from both hospitals to realize the relevance, sequence, skip pattern, completeness and consistency of checklist. Two experienced BSc nurse and two ART data supervisors were assigned as data collectors and supervisors respectively for each hospital. Two days training was given for data collectors and supervisors on the aim of study, where to collect patient's data, developed data extraction format and mobile data collection by using Kobo Toolbox. The qualities of data assured by cross checking sources of data. During data collection, data collectors are responsible to complete data on extraction format deployed to kobo collect application on their smart phone and send to server. Preparedness of all necessary data source were facilitated and assured by supervisors. Overall activity of study was closely monitored by principal investigator.

4.10. Data Entry and Analysis

Collected data checked on Kobo toolbox by principal investigator. Data saved on Kobo Toolbox was exported to excel, then extracted to SPSS. By using SPSS version 26, data was recoded and cleaned. Before started data analysis each variable were checked for accuracy, outliers, miss values and consistencies by running frequencies. Patients who have VL test result less than 1000 copies/ml at least in one repeat test result during 12 months follow up periods is considered to

the outcome. Time to viral load suppression was calculated from a date of first blood sample drawled to date of last repeat VL test result register at ART clinic.

Explored descriptive analysis by using median, inter-quartile range, mean, standard deviation, proportions and normality distribution for all explanatory variables accordingly. Kaplan-Meier was used to estimate time to viral load suppression and log-rank test carried out to compare the difference between the survival curves for unequal follow-up times of study participants. The Cox-proportional hazard model was used to identify independent predictors of viral suppression. Before exploring the model, multi-colinearity was checked. The proportional hazard assumption was assessed based on log minus log. Variables with p-value ≤ 0.25 in the bivariate model were candidate to the multivariate Cox proportional hazards model analysis. By using backward stepwise procedure, candidate variables were enter to multivariate cox-proportional hazard model to check confounding, interaction and identify independent predictors of time to viral load suppression. Predictors with p-value less than 0.05 were included in the final model. The crude and adjusted hazard rate computed and interpreted together with their corresponding 95% confidence intervals.

4.11. Operational Definitions or definitions terms

Routine viral load monitoring: It is a viral load test done at regular time interval to determine change in viral load for HIV patients on ART. (4).

Viral load suppression: Was considered when viral load is less than or equal to 1000 copies/ml, on a routine viral load test (4).

Event: Viral load suppression

Censored: Patient with unsuppressed viral load (viral load of>1000 copies/ml) on a routine viral load test, Lost Follow-up, transfer out, switch to second line and died before the end of the follow-up period.

Time to viral suppression: It is time from high viral load result registered on ART registration to the last at least one viral load result less than 1000copies/ml. It was calculated by subtracting the month of high viral load detected from the month of the suppression registered or censored.

Incidence Rate: Number of participant's experienced VL suppression during follow up period divided by sum of months of each study participants was at risk of experiencing VL suppression and it expressed by person-month.

Transfer out: Moving by taking the full medical record from study area to other health institution or within clinic for care and treatment

Lost Follow-up: Not visited ART clinic for 3 month and for whom vital status (alive or dead) is not already.

.**Incomplete record:** It was considered when the indicator of the dependent variable and/or the independent variable is not registered.

Functional Status: was categorized as working- patient with capable of going out of home and do routine activities, ambulatory- patient with capable of self-care and going to the toilet unsupported and bedridden- patient who cannot go even to the toilet unsupported (3).

Opportunistic infections: illness caused by HIV patients with high viral load. It was classified as yes or no.

Baseline CD4 counts: it is the nearest CD4 cell count before high viral load detected. It was categorized as <200cell/mm^3, 200-350cell/mm^3 and >350cell/mm^3.

Body-Mass-Index (BMI): It is calculated by dividing the weight in kilogram with height in meters squared. It was categorized as WHO classification, Obesity (>=30kg/m2), over weight (25-29.99kg/m2), normal (18.5-24.99kg/m^2), mild (17-18.49kg/m2), Moderate (16-16.99kg/m2), and severe malnourished (<16kg/m^2).

Drug adherence level: it is the percentage of ARV drug taken by patient. It was categorized as good defied as >=95%, fair defied as 85%-94% and poor defied as <84% of doses taken according to instruction given by the care providers.

Social problem: patient who had no treatment supporter. It was classified as yes or no

Substance use: study participants who had at least one history of drink alcohol, smoke cigarette and chew chat after diagnosed with high viral load classified as yes or no.

EAC session: It is every month follow schedule by using structured sheet form for assessment of current level adherence and to address the specific barriers of drug adherence after HIV patient diagnosed to high viral load.

Duration on ART: It was calculated by subtracting the months enrolled to ART from months of high viral load detected. It was categorized as less 12months, 13-24months, and 25-59months and above 60months.

Baseline viral load: It was categorized as 1000-5000, 5001-10,000 and >10,000.

4.12. Ethical Considerations

Ethical clearance was obtained from the Institutional Review Board of College of Medicine and Health Sciences of Hawassa University before conducted study. After securing ethical clearance from Institutional Review Board of Hawassa University, Bule Hora and Dilla University Referral Hospital was informed about the objective of the study through a support letter from Hawassa University School of Public Health. Formal letters were obtained from both university referral hospital administration offices before started data collection. Informed consent was not needed because patients might not access in time data collection day. To keep the confidentiality personal identifiers were not included in the data extraction format.

5. Results

5.1. Baseline Socio-Demographic characteristics of the study subjects

A total of 344 HIV infected patients with high viral load and initiating to ART from January 2016 to December 2022 were enrolled to study. The data were retrieved from ART logbook, patient follow up medical record, EAC sheet and electronic data base for measurements. Of these 180 (52.3%) were from Bule Hora teaching hospital and 164 (47.7%) were from Dilla teaching hospital.

The median and Inter quartile range for the age of cohort were 34 and 28-40 years, respectively, and One hundred thirty (37.8%) of study participants were in age group 25-34 years. Approximately to one-third (32.6%) of participants were completed secondary education level. Of participants 202 (58.7%) were female and 133 (38.7%) were married. Twenty four (7%) and fifth seven (16.6%) of study participants were governmental employ and house wife respectively. Concerning religion of study participants 156 (45.3%) were orthodox followers (Table 2).

Table 2: Baseline Socio-Demographic characteristics of the high viral load adult HIV patients on ART at Southern Ethiopia, in 2016-2022 (N = 344).

Variables	Categories	Frequency	Percent
ART Sites	Bule Hora Hospital	180	52.3
	Dilla Hospital	164	47.7
Sex	Male	142	41.3
	Female	202	58.7
Age	15-24 age	45	13.1
	25-34 age	130	37.8
	35-44 age	111	32.3
	45+ age	58	16.9
Educational status	Can’t read and write	79	23.0
	Primary education	101	29.4
	Secondary education	112	32.6
	Tertiary	52	15.1

Continues…

Variables	Categories	Frequency	Percent
Marital status	Single	108	31.4
	Married	133	38.7
	Separated	27	7.8
	Widowed	36	10.5
	Divorced	40	11.6
Occupation	Farmer	46	13.4
	House wife	57	16.6
	Merchant	53	15.4
	Government employ	24	7
	None government employ	48	14
	Daily laborer	55	16
	No job	34	9.9
	Other job	27	7.8
Religion	Protestant	152	44.2
	Orthodox	156	45.3
	Muslim	19	5.5
	Catholic	6	1.7
	Others	11	3.2

5.2 Clinical related characteristics of the study subjects

More participants of study 270 (78.5%) were able to perform usual work in or out of their house (working). About 153 (54.7%) and 29 (26.7%) had history of opportunistic infection and less than 200cell/Iu count CD4 in their blood. One hundred ninety nine (57.0%) of patients had WHO clinical stage one. Around two-third (64.5%) of patients had normal BMI. Two-third (59.3%) of study participants had greater than 10,000 copies/ml baseline viral load (Table.3).

Table 3: Clinical related characteristics of the high viral load adult HIV patients on ART at Southern Ethiopia in 2016-2022 (N = 344).

Variables	Categories	Frequency	Percent
Functional status	Working	270	78.5
	Ambulatory	52	15.1
	Bed ridden	22	6.4
Opportunistic Infection	Yes	188	54.7
	No	156	45.3

Conti…

Variables	Categories	Frequency	Percent
Baseline CD4 cell counts	<200cell/iu	92	26.7
	200-350cell/iu	131	38.1
	>350cell/iu	121	35.2
WHO clinical stage	Stage I	196	57
	Stage II	68	19.8
	Stage III	58	16.9
	Stage IV	22	6.4
BMI	Normal	222	64.5
	Mild	122	35.5
Baseline high VL	1000-5000copies/ml	75	21.8
	5001-10000copies/ml	65	18.9
	>10000copies/ml	204	59.3

5.3 Anti-Retro viral and other preventive therapy related characteristics of the study subjects.

Majority 134 (39%) and 118 (34.3%) of study participants were on ART for 25-59months and 13-24 months respectively. Approximately two-third (60.8%) of study participants were on TDF+3TC+DTG and 103 (29.9%) on TDF+3TC+EFV drug types at the end of study. Among study participants 165 (46.5%) had history of drug changes. From study participant 209 (60.8%) had experience of any type of drug side effects. Two-third (67.7%) of study participants were received Cotrimoxazole-preventive therapy and 226 (65.4%) were used Isoniazid-preventive therapy at baseline. More of study participant 152 (52.9%) were good adherence to drug treatment at end (Table 4).

Table 4: Anti-Retro viral and other preventive therapy related characteristics of the high viral load adult HIV patients on ART at Southern Ethiopia in 2016-2022 (N = 344).

Variables	Categories	Frequency	Percent
Duration on ART	Less than 12 Months	76	22.1
	13-24 Months	118	34.3
	25-59 Months	134	39
	60 Months and above	16	4.7
ART drugs regimen	TDF+3TC+DTG	209	60.8
	TDF+3TC+EFV	103	29.9
	TDF+3TC+NVP	15	4.4
	AZT-3TC-EFV	17	4.9

Conti…

Variables	Categories	Frequency	Percent
History of drug change	Yes	160	46.5
	No	184	53.5
Drugs side effect	Yes	135	39.2
	No	209	60.8
Baseline CPT prophylaxis	Yes	233	67.7
	No	111	32.3
Baseline INH prophylaxis	Yes	225	65.4
	No	119	34.6
Drug Adherence level	Good	182	52.9
	Fair	86	25
	Poor	76	22.1

5.4 Psychosocial and Service related Characteristics of the Study Subjects.

All study participants were enrolled to EAC session with them of 15 (4.4%) and 196 (57.8%) attended one and three session respectively. More than half (55.2%) study participants were disclosed their HIV status for other persons. Among study participants one hundred eighty six (54.1%) of patients were use reminder to take their drugs on time. Out of study participants 143 (41.6%) participants were substance user. Only 96 (27.9%) of study participants had social problem (Table 5).

Table 5: Psychosocial and other characteristics of patients on ART at Southern Ethiopia, 2016-2022 (N = 344)

Variables	Categories	Frequency	Percent
Attended number of EAC	One	15	4.4
	Two	103	29.9
	Three	196	57
	Four and above	30	8.7
HIV disclosure status	Disclosed	190	55.2
	Not disclosed	154	44.8
Use reminder to take drug	Yes	186	54.1
	No	158	45.9
Substance use	Yes	143	41.6
	No	201	58.4
Social problem	Yes	96	27.9
	No	248	72.1

5.5. Patients follow up in cohorts

5.5.1. Time to viral load suppression

All of the 344 study participants were followed for a median (Inter quartile range) 5 (4-7) months with total of 1823 person-months. For this study the overall median time to viral suppression was 5months (95% CI: 4.65, 5.34). The of viral load suppression were achieved on 280 (81.4%; 95% CI: 77%, 86.5%), of the patients at the end of follow up period. The overall incidence rate of viral load suppression was 15.3 per 100 person-months with (95% CI: 10.9, 18.43 per 100 person-months) after diagnosed with high viral load.

5.5.2. Comparison of time to viral load suppression

The Kaplan-Meier analysis and log-rank test were used to observe the difference in viral load suppression on time based among category of predictor variables.

Survival distribution for different CD4 cell count categories shows there are significant difference among them. Time to viral load suppression was greater for 200cell/mm3 (P = 0.001) (Figure2). Time to viral suppression was shorter for study participants with no opportunistic infection (P = 0.001) (Figure3). There is significant difference of time to viral load suppression among patient received TDF+3TC+DTG, TDF+3TC+EFV, TDF+3TC+NVP and AZT-3TC-EFV (P = 0.001) (Figure 4). Time to viral load suppression was higher for substance user than not users (P 0.001) (Figure 5). Minimum time to viral load suppression was observed in patient who had ART duration less than 12month on ART when compared with other categories of ART duration users (P 0.001) (Figure:6). Other significant difference of time to viral load suppression was observed in category of Sex, functional status, WHO clinical stage, BMI, Baseline viral load, ART drug substitution, drug side effect, Isoniazid-preventive therapy, ART adherence, Use reminder, and Attended number of EAC. However the p-value of log-rank was not identify the existence of significant difference of time to viral load suppression among categories of Age, Marital status, Educational status, Occupation, Religions, Cotrimoxazole-preventive therapy, HIV disclosure and Social problems.

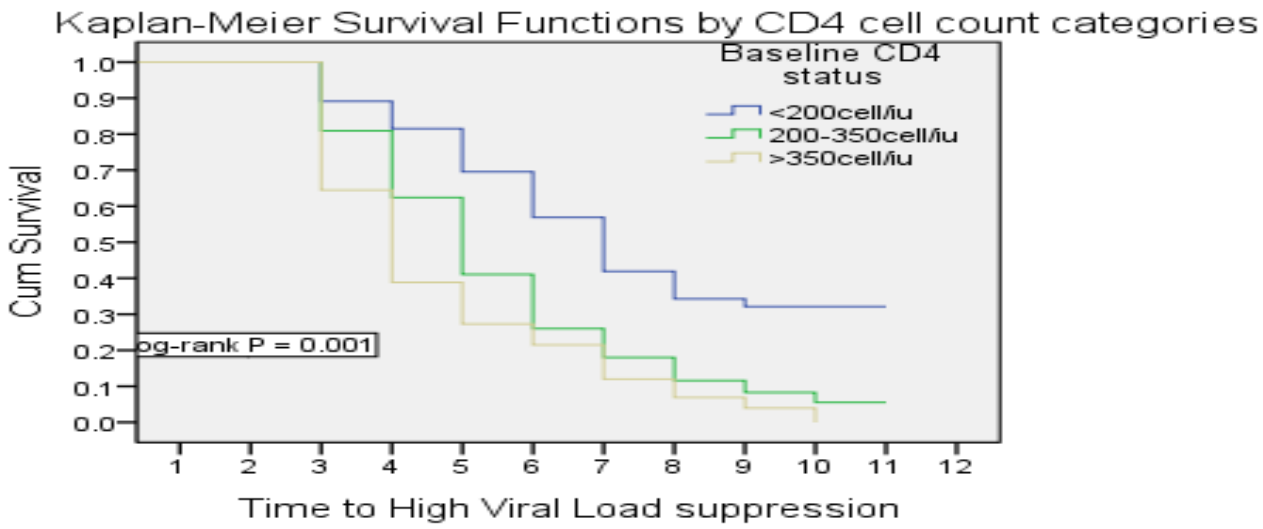

Figure2: Kaplan-Meier estimate of high viral load free survival with CD4 categories in high viral load adult HIV patients on ART at Southern Ethiopia in 2016-2022.

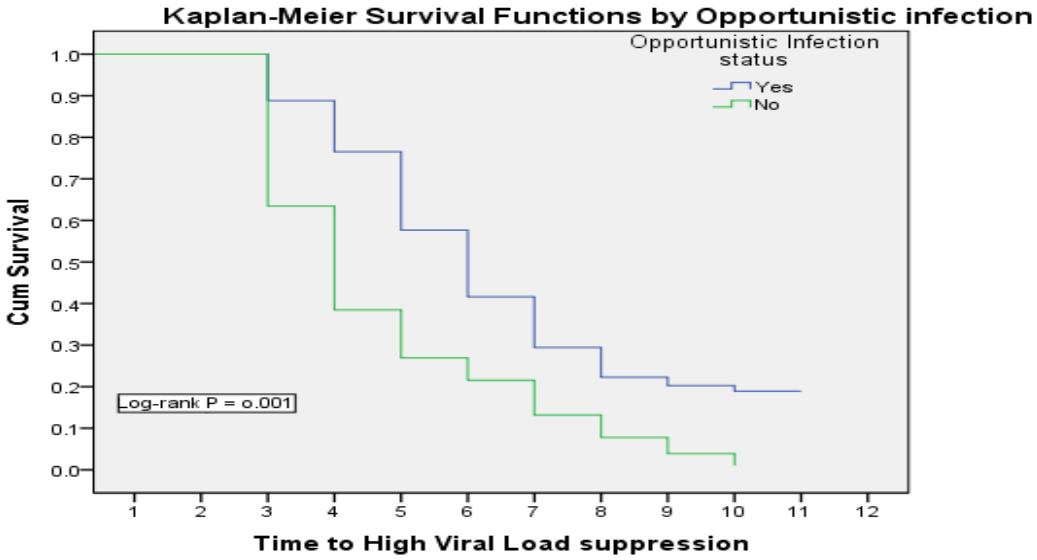

Figure3: Kaplan-Meier estimate of high viral load free survival with opportunistic infection in high viral load adult HIV patients on ART at Southern Ethiopia in 2016-2022.

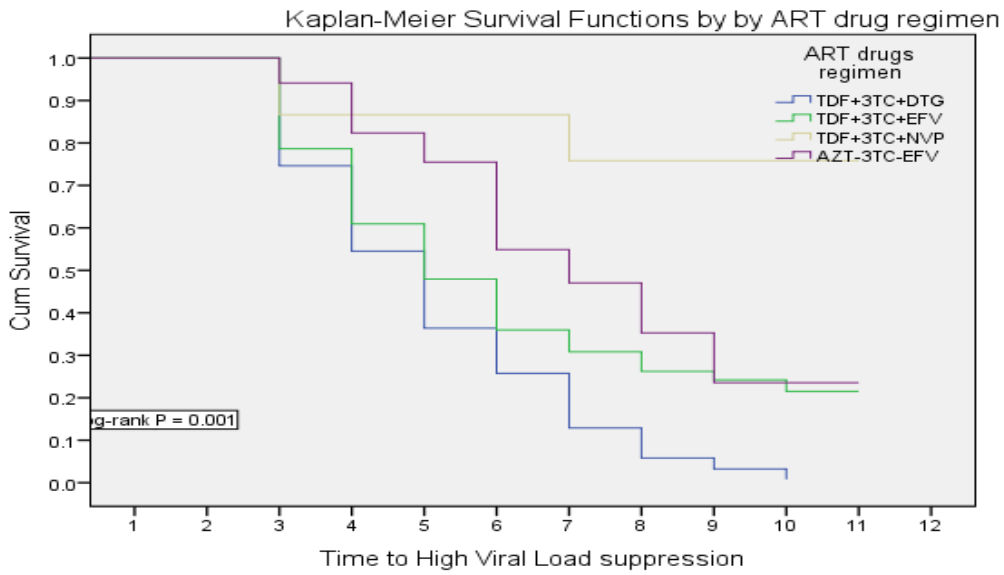

Figure 4: Kaplan-Meier estimate of high viral load free survival with ART drug regimen in high viral load adult HIV patients on ART at Southern Ethiopia in 2016-2022.

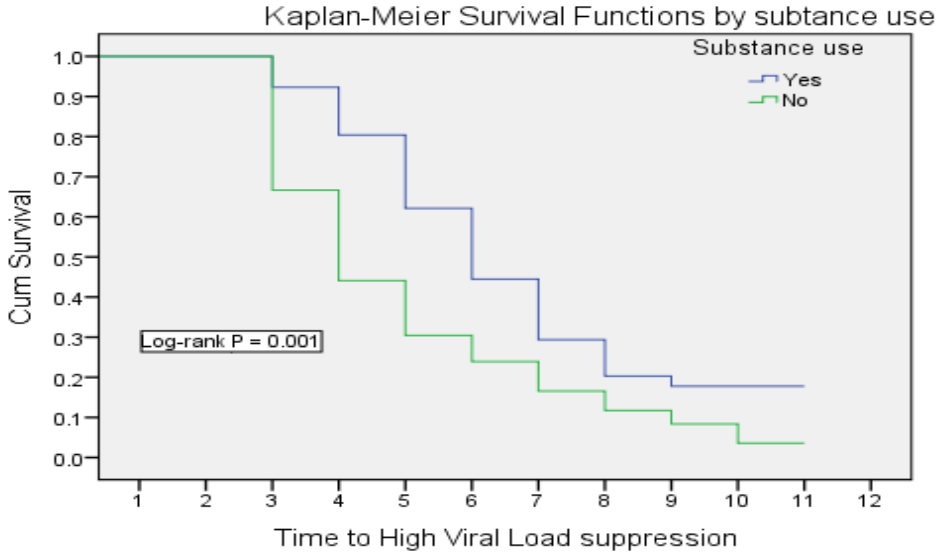

Figure 5: Kaplan-Meier estimate of high viral load free survival with substance use in high viral load adult HIV patients on ART at Southern Ethiopia in 2016-2022.

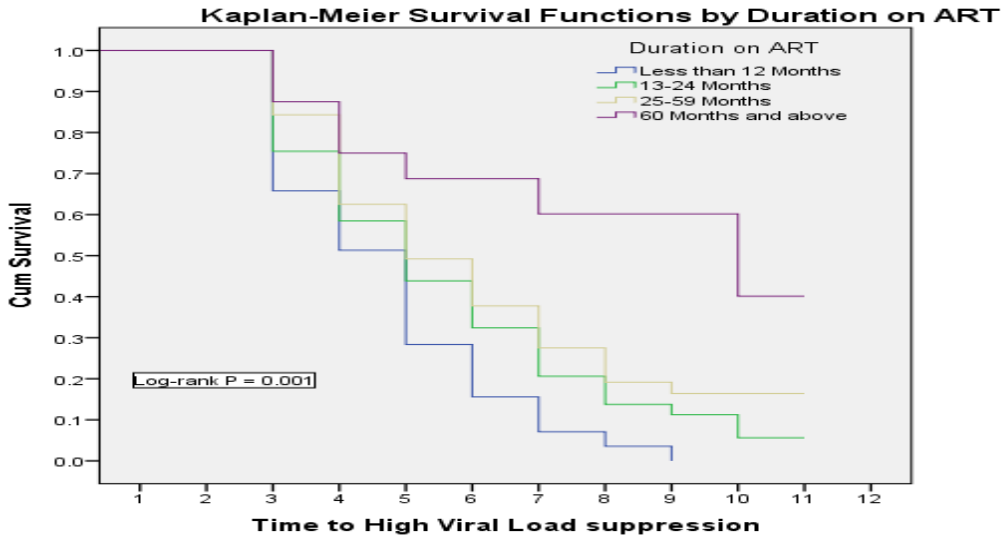

Figure 6: Kaplan-Meier estimate of high viral load free survival with Duration on ART in high viral load adult HIV patients on ART at Southern Ethiopia in 2016-2022.

5.5.3. Predictors of viral load suppression.

The result of the bivariate analysis showed that variables such as functional status, BMI, baseline viral load, WHO clinical stage, ART drug regimen, isoniazid prophylaxis, ART drug adherence, ART duration, and used reminder to take ART drug were significantly decrease the chance of viral load suppression when compared with their reference category. On other hand predictors likes no opportunistic infection, ART drug side effect, CD4 count categories, and no substance use were significantly increase the chance of viral load suppression when compared with their reference category (Table 6). .

However, in multivariable analysis only five variables such as having opportunistic infection, baseline CD4 counts, ART dugs regimen, duration on ART and substance use were independent predictors of high viral load suppression after controlling for others factors. Patients who were without opportunistic infection had 1.44 times more likely suppressed their viral load than those with opportunistic infection (AHR: 1.44; 95% CI: 1.06, 1.96). Patients who did not use substances had 1.54 times higher chance of achieving viral load suppression than who did use substances (AHR: 1.54; 95% CI: 1.19, 1.99). Similarly patient with higher CD4 counts 200-350 cells/mm3 had 1.75 times and >350cells/mm3 had 1.53 times more likely suppressed their viral load compared to patients with lower CD4 counts <200cell/mm3 (AHR: 1.75; 95% CI: 1.24, 2.45 and AHR: 1.53; 95% CI: 1.02, 2.28). The HIV patients who were received the drug regimens TDF+3TC+NVP had 0.21 times or AZT-3TC-EFV 0.50 times less likely achieved viral load suppression compared to patients who were received the TDF+3TC+DTG regimen (AHR: 0.21; 95% CI: 0.07, 0.68, and AHR: 0.50; 95% CI: 0.26, 0.96). Patients who were on ART for longer durations 13-24 months (AHR: 0.72; 95% CI: 0.53, 0.98), 25-59 months (AHR: 0.68; 95% CI: 0.50, 0.93) and above 60 months (AHR: 0.26; 95% CI: 0.12, 0.58) were less likely achieved viral load suppression compared to patients who were on ART for less than 12 months (Table 6).

Table 6: Bivariate and Multivariate Cox of the high viral load adult HIV patients on ART at Southern Ethiopia in 2016-2022 (N = 344).

Variables	Viral load suppression status		CHR (95%.CI)	AHR (95%.CI)
	Unsuppressed # (%)	Suppressed # (%)		
Sex				
Male	32 (9.3)	110 (32.0)	1	1
Female	32 (9.3)	170 (49.4)	1.31 (1.03,1.67)	1.13 (0.88,1.44)
Educational status				
Can't read and write	22 (6.4)	57 (16.6)	1	1
Primary education	16 (4.7)	85 (24.7)	1.41 (1.01,1.97)	1.21 (0.84,1.75)
Secondary education	15 (4.4)	97 (28.2)	1.46 (1.05,2.03)	1.2 (0.84,1.7)
Tertiary	11 (3.2)	41 (11.9)	1.31 (0.88,1.96)	1.07 (0.68,1.68)
Functional status				
Working	30 (8.7)	240 (69.8)	1	1
Ambulatory	20 (5.8)	32 (9.3)	0.49 (0.34,0.71)	0.75 (0.49,1.13)
Bed ridden	14 (4.1)	8 (2.3)	0.26 (0.12,0.53)	0.65 (0.3,1.4)
Opportunistic Infection				
Yes	56 (16.3)	132 (38.4)	1	1
No	8 (2.3)	148 (43.0)	1.97 (1.55,2.5)	1.44 (1.06,1.96)**
CD4 cell count				
<200cell/iu	40 (11.6)	52 (15.1)	1	1
200-350cell/iu	21 (6.1)	110 (32.0)	2.04 (1.46,2.85)	1.75 (1.24,2.45)**
>350cell/iu	3 (0.9)	118 (34.3)	2.78 (2,3.86)	1.53 (1.02,2.28)**
WHO clinical stage				
Stage I	23 (6.7)	173 (50.3)	1	1
Stage II	13 (3.8)	55 (16.0)	0.77 (0.57,1.05)	1.15 (0.78,1.71)
Stage III	15 (4.4)	43 (12.5)	0.62 (0.44,0.87)	1.24 (0.79,1,96)
Stage IV	13 (3.8)	9 (2.6)	0.26 (0.13,0.51)	0.72 (0.34,1.54)
BMI				
Normal	33 (9.6)	189 (54,9)	1	1
Mild malnourished	31 (9.0)	91 (26.5)	0.72 (0.56,0.92)	0.89 (0.67,1.18)
Baseline high VL				
1000-5000copies/ml	8 (2.3)	67 (19.5)	1	1
5001-10000copies/ml	5 (1.5)	60 (17.4)	1.18 (0.84,1.68)	1.24 (0.86,1.80)
>10000copies/ml	51 (14.8)	153 (44.5)	0.71 (0.53,0.94)	0.99 (0.72,1.36)
Duration of ART				
Less than 12 Months	3 (0.9)	73 (21.2)	1	1
13-24 Months	18 (5.2)	100 (29.1)	0.69 (0.51,0.94)	0.72 (0.53,0.98)**
25-59 Months	34 (9.9)	100 (29.1)	0.57 (0.42,0.77)	0.68 (0.50,0.93)**
60 Months and above	9 (2.6)	7 (2.0)	0.25 (0.11,0.55)	0.26 (0.12,0.58)**

Cont…

Variables	Viral load suppression status		CHR (95%.CI)	AHR (95%.CI)
	Unsuppressed # (%)	Suppressed # (%)		
Baseline ART drugs				
TDF+3TC+DTG	15 (4.4)	194 (56.4)	1	1
TDF+3TC+EFV	30 (8.7)	73 (21.2)	0.64 (0.50,0.85)	0.77 (0.58,1.02)
TDF+3TC+NVP	12 (3.5)	3 (0.9)	0.13 (0.04,0.40)	0.21 (0.07,0.68)**
AZT-3TC-EFV	7 (2.0)	10 (2.9)	0.43 (0.23,0.82)	0.50 (0.26,0.96)**
History of ART drug change				
Yes	36 (10.5)	124 (36.0)	1	1
No	28 (8.1)	156 (45.3)	1.25 (0.99,1.58)	1.22 (0.95,1.58)
Drug side effect				
Yes	39 (11.3)	96 (27.9)	1	1
No	25 (7.3)	184 (53.5)	1.53 (1.19,1.97)	1.19 (0.93,1.54)
Baseline Isoniazid-preventive therapy				
Yes	35 (10.2)	190 (55.2)	1	1
No	29 (8.4)	90 (26.2)	0.74 (0.58,0.96)	0.88 (0.67,1.14)
ART drugs Adherence				
Good	27 (7.8)	155 (45.1)	1	1
Fair	22 (6.4)	64 (18.6)	0.82 (0.61,1.10)	0.85 (0.62,1.16)
Poor	15 (4.4)	61 (17.7)	0.74 (0.55,0.99)	0.92 (0.67,1.25)
Use reminder to take drug				
Yes	25 (7.3)	161 (46.8)	1	1
No	39 (11.3)	119 (34.6)	0.76 (0.56,0.96)	1.15 (0.89,1.5)
Substance user				
Yes	40 (11.6)	103 (29.9)	1	1
No	24 (7.0)	177 (51.5)	1.80 (1.41,2.3)	1.54 (1.19,1.99)**

** = significant at multi-variables

6. Discussion

In this study, good (81.4%) viral load suppression was achieved during study period. The median time to viral suppression was 5 months. The overall incidence rate of viral load suppression was 15.3 per 100 person-months. Opportunistic infection, baseline CD4 counts, ART dugs regimen, duration on ART and substance use were independent predictors of high viral load suppression after controlling for others potential confounding variables.

The viral load suppression proportion of this study was higher than the reported proportion from three study conducted in different region of Ethiopia. According such studies the proportion of viral suppression was 66.4%. 64% and 40.9% respectively (13,15,29). On other hand this finding was low as compared to the result of studies done to evaluate the impact of EAC on viral load suppression among HIV patients on first-line regimens with high viral load in India and Nigeria with 88% and 90% observed proportion respectively (27,28). The observed difference might be due to different follow up duration and quality of ART drugs during study period. In this study the study participants were followed for maximum twelve months while the study participants in other studies followed for three to six months. The finding of this study was similar with studies in western Ethiopia with 79.7%, and WHO updated guideline of ART drugs in 2021 reveals, the proportion of viral load suppression was vary from 70% to 87% among HIV patients with high viral load before diagnosed for first-line treatment failure (4,10).

The result of this study reveals the overall incidence rate of high viral load suppression was 15.3 per 100 person- month. The finding of this study was higher than the incidence rate observed in study conducted in West Gojjam zone, Amhara region of Ethiopia with 11.17 per 100 Persons-Month, and Nigist Eleni Mohammed memorial comprehensive specialized Hospitals southern Ethiopia with 9.3 per 100 Persons-Month (13,30,31). The variation of incidence among studies might be explained due to study period

In this study, the overall median time of high viral load suppression was 5 months. This result is consistence with retrospective cohort study conducted in Northern Ethiopia with median time to viral load suppression was 5 months (95% CI; 4-6) and WHO estimation between 3 -6 months of

high viral load suppression (4,13). But lower than the result of studies conduct in Uganda and Kenya of median time to suppression was 24 weeks and 6 month respectively (18,30). This indicated the country adhere to WHO HIV treatment guideline and on good way to meet three 95% global target at the end 2030. But the observed difference may be due to follow up period and the two countries may follow different in management systems of high viral load HIV patients.

The present study showed that patient with no opportunistic infection was independently associated with more likely achieved viral load suppression than those patients with opportunistic infection. This was supported by the result of study conducted in Ethiopia, South Africa and Uganda, with Adjust hazard rate of, 1.85 times, 1.85 times and 1.09 times higher for patient who had no opportunistic infection respectively (13,22,35,40). This was might be explained by the truth that patients who had acquired opportunistic infection had low immunity and increased the rate of viral replication when compared with none opportunistic infection patients.

In this study, patients with baseline CD4 cell counts 200-350cell/mm3 and more than 350cell/mm3 were higher likely suppressed their viral load than patient with CD4 count less than 200cell/mm3. This finding was similar with the study results of southern and Northern Ethiopia and South Africa with AHR 2.76 and1.98 with ($P < 0.05$) respectively (10,13,32,35). It is well known that CD4 cell count has opposite relation-ship with viral replication. As the number of CD4 counts increased, the rate of viral replication is declines which have advantage's to increase the immunity of patients explained by decreased the occurrence of opportunistic infection.

Similarly current study participants who have no history of substance use were independently significant higher viral load suppression when compared with those participants with history of substance use. This was supported by the reported result from studies conducted in Southern Ethiopia, South Western Uganda, Canada and America states that overall patient who had not used substance were more likely achieved viral load suppression than those patients who had used substance ($p < 0.05$), (34,37–39).

On other hand the finding of this study was indicated patient who were received, ART drugs regimen TDF+3TC+NVP and AZT-3TC-EFV had less likely achieved viral load suppression as compared to patient received TDF+3TC+DTG ART drug regimen when controlled for others. The finding of this study in line with the study finding from Northern Ethiopia reveals patients received NVP based regimen had lower achievement of viral load suppression when compared with patients received EFV-based regimen (P <0.001)(32). Similarly, study from Southern Ethiopia indicated, that participant received NVP and EFV-based regimens had lower viral load suppression than participant received PI-based regimen by (95% CI: 54%, 97%) and (95% CI =21%,94%) respectively(15). The finding of this study was also supported by the finding of study from Cameroon with significantly higher observed of viral load suppression in TDF+3TC+EFV regimen combination than other combination included NVP and AZT (P < 0.05) (23). Finally the study from Oxford university was in line with our study by reveals that viral load suppression in patient on DTG based therapy was 1.2 times higher (AHR=1.2; 95% CI, 1.0,1.4) when compared with others (36).

Another important predictor in this study was, duration on ART. Patient who were alive for more than 60months, 25-59months and 13-24maths on ART had less likely suppressed viral load when compared with patients for less than 12months duration. The result of this study was consistent with result of studies from Ethiopia, Cameroon, and India shows as the overall viral load suppression was significantly decreased as increased duration of patients on ART (P < 0.05) (14,23,27). This might be explained by the patients with length of time on ART, which may deteriorate immunological condition. Additionally, CD4 cell destruction over time and patient diagnosed in recent calendar years were managed with high quality of care and potent drugs that focused on maintain good drug adherence and lower side effect lead to drug change.

7. Strength and limitation of study

7.1. Strength

- This study used standardized kobo toolbox during data collection for maintain the quality of data collection.'
- Inclusion of most important predictor's variables of viral suppression likes ART drugs regimens and substance use and variables that absent association with viral load suppression such as social problems, use reminder to take drugs and BMI.
- The follow up time of this study was relatively longer and include data from many point of years when compared with other study.

7.2. Limitation

- The finding of this study was based on secondary data which not easy to get full data records and exclude that patient with incomplete data records,
- Some variables like income level and mental problem were not included in medical records.

8. Conclusion

In conclusion, majority (81.4%) of study participants achieved viral load suppression in the study area. Incidence of viral suppression was 15.3 per 100 person- months. The median survival time of high viral load in this study was 5 months. Absence of opportunistic infection, high baseline CD4 cell counts of above 200cells/mm^3, not use substance were associated with higher viral load suppression. TDF+3TC+NVP and AZT-3TC-EFV ART drugs regimens and length of duration on ART more than 60months, 25-59months and 13-24maths were independently associated with lower viral load suppression.

9. Recommendation

Health care providers should have considers for:

- The patients with opportunistic infections, those who use substances, and those with lower CD4 counts may require closer monitoring and support to achieve viral load suppression
- The choice first line ART drug regimens with TDF+3TC+DTG or TDF+3TC+EFV, as TDF+3TC+NVP and AZT-3TC-EFV were associated with less viral load suppression in this study
- HIV patients on treatment for the long term.

ART case managers and multidisciplinary teams should focused to strength assessment and counseling, which important to reduce opportunistic infection, effective treatment outcome, behavioral and psychological support for substance users of high viral load HIV patient. National HIV programmers should prioritize to introduce point of care viral load testing system which recommended by WHO in order to improve the immediate test result, which is helps health care providers, ART case managers and multidisciplinary teams to take early action to reduce clinical, behavioral and psychological problem of high viral load HIV patient.

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11. Annex

Annex I. Data Collection Format

Data collection format for Hawassa University, MPH research project on time to viral load suppression and its predictors on HIV infected patients with high viral load, in Bule Hora and Dilla University Referral Hospital, 2016-2022.

Part I. Study subject's baseline information (to be filled from ART clinic intake form)

Section 1: Socio-Demographic Characteristics

No	Variable	Coding categories	Remark
101	Patient unique ART Number	_____	
102	ART site	1.Bule Hora Hospital 2.Dilla Hospital	
103	Date confirmed HIV positive	_____	DD/MM/YYYY. E.C
104	Date of first ART initiation	_____	DD/MM/YYYY. E.C
105	Age of patient	_____	
106	Sex of patient	1.Male 2. Female	
107	Marital status	1.Never married 2.Married 3.separated 4.Divorced 5.widowed	
108	Educational status	1.No education 2.primary 3.Secondary 4.Tertiary	
109	occupational	1.Farmer 2.Merchant Governmental 3.employee 4.Non-governmental Employee 5.Day laborer 6.Jobless 7.driver 8.Others(specify)_____	

110	Religious	1.Muslim 2.Orthodox 3.Protestant 4.Catholic 5.others (specify)_____	

Section II: Base line clinical, laboratory and ART information

201	Functional status	1.Working 2.Ambulatory 3.Bedridden	
202	Base line opportunistic infection	1.Yes 2.No	
203	Base line WHO clinical stage	1.Stage I 2.Stage II 3.Stage III 4.Stage VI	
204	Base line CD4 counts	_____	
205	Height (meters)	_____	
206	Base line Weight(kg)	_____	
207	Baseline High viral load	_____copies/mm^3	

Section 3: ART and treatment

301	Base line first line treatment drugs	1.TDF+3TC+DTG 2.TDF+3TC+EFV 3.TDF+3TC+NVP 4.AZT-3TC-NVP 5.AZT-3TC-EFV 6.ABC+3TC+EFV 7.ABC+3TC+LPV/r 8.Other specify_____	
302	Drugs changes during treatment	1.Yes 2.No	
303	Did Patient develop severe ARV drugs side effects in the past?	1.Yes 2.No	
304	Co-trimoxazole preventive therapy at base line	1.Yes 2.No	
305	Base line Isoniazid TB preventive therapy	1.Yes 2.No	
306	Base line Adherence level for ART	1. Good 2. Fair 3. Poor	

Part II: Patient's follow up information

Please document the current or the recent results

Section Iv: Psychosocial and others predictors

401	Total Number of EAC session attended by patients	_____	If attended number is zero skip to Ques. No 403
402	Date of first EAC session start	_____	
403	Did patient disclosed HIV status to anyone?	1.Yes 2.No	
404	Did patient uses Reminder to take ART drugs	1.Yes 2.No	
405	Did patient Regularly take substance abuse?	1.Yes 2.No	
406	Have patient social problem?	1. yes 2. No	social support, disclosure, stigma,

			&poor living condition

Section I: outcome variable

No	Variable	Coding categories	Remark
501	Date of blood sample drawn for last viral load result	_____	
502	Date of last repeat VL result register on patient registration book	_____	If no second or last VL result skip to 505
503	last repeat VL result	_____copies/ml	
506	Last Date of patient visit/ known as on ART	_____	
504	Patient at end /last visit of follow up	1. Active 2. Switch second line regimens 3. Lost to follow up 4. Transfer out 5. Dead	