

Saint Paul's Hospital Millennium Medical College

Department of Public Health

Ethiopian Field Epidemiology and Laboratory Training program



Research Report on

Factors Associated with Virological Non-suppression among HIV Positive Patients on Highly Active Antiretroviral Therapy in Public Hospitals, Addis Ababa, Ethiopia

Kinfu Manzura (MD, 2nd Year EFETP Resident)

**Submitted to Saint Paul's Hospital Millennium Medical College (SPHMMC)
Department of Public Health for Partial Fulfillment of MPH in Field
Epidemiology**

September 2019

Addis Ababa, Ethiopia

Research Report on
Factors Associated with Virological Non-suppression among HIV
Positive Patients on Highly Active Antiretroviral Therapy in Public
Hospitals, Addis Ababa, Ethiopia

Kinfu Manzura (MD, 2nd Year EFETP Resident)

Primary Advisor:

Yoseph Worku (MD, MPH)

Co-advisor:

Aman Yesuf (MPH)

Submitted to Saint Paul's Hospital Millennium Medical College (SPHMMC)
Department of Public Health for Partial Fulfillment of MPH in Field
Epidemiology

September 2019

Addis Ababa, Ethiopia

Acknowledgements

I am grateful to Federal Ministry of Health and Saint Paul's Hospital Millennium Medical College for giving me the opportunity to study field epidemiology. I am also grateful to EPHI for coordinating our field base and to CDC for their technical assistance.

I am also grateful to Dr Yoseph Worku for reviewing this document and giving me constructive comments.

My special thanks go to my parent, my wife and my baby boy for their special contribution for my academic work.

Finally I would like to thank all ART adult outpatient department staffs of Saint Paul's Hospital Millennium Medical College, Zawditu Hospital and Yekatit 12 Hospital, and all my peers.

Abstract

Background

In Ethiopia approximately 1.3 million people live with HIV. Even though the number of people accessing antiretroviral therapy (ART) has gradually increased in the recent years the goal of attaining virologic suppression is not yet achieved. The objective of the study was to determine the factors associated with virologic non-suppression among HIV +ve patients on Highly Active Antiretroviral Therapy (HAART) in public hospitals, Addis Ababa, Ethiopia.

Methods and Materials

A 1:3 unmatched case control study was conducted starting from June 24, 2019 to July 19, 2019. 100 virologically non suppressed and 300 virologically suppressed HIV +ve patients were included and admitted and critically ill HIV +ve patients were excluded. Data was collected using questionnaires, entered using Epi-Info v 7.1 and analyzed using SPSS version 23. After ‘simple’ binary logistic regression, ‘multiple’ binary logistic regression analysis was carried out to identify the independent determinants of virological non suppression. We used $p \leq 0.05$.

Result

A total of 400 study participants (100 virologically non-suppressed and 300 virologically suppressed) participated in this study. The mean age of cases and controls was 37yrs and 43 yrs respectively. The mean duration on HAART of cases and controls was 106 months and 115 months respectively. Factors associated with virologic non suppression were age <35yrs (AOR=11.9, 95%CI 2.2-66.6), initial viral load ≥ 1000 copies/ml (AOR=324.0, 95%CI 66.2-1585.9) and poor/fair adherence (AOR=9.2, 95%CI 3.2-26.7).

Conclusion

This study showed that age <35yrs, initial viral load ≥ 1000 copies/ml and poor/fair adherence is predictors of virological non suppression. Therefore, efforts should be strengthened to improve adherence to ART, which helps to suppress viral replication and load. Additionally, it is important to give more attention to younger (<35yrs) patients.

Key words: HIV, Virologic non-suppression, case-control, Addis Ababa, Ethiopia

Contents

Acknowledgements.....	i
Abstract.....	ii
List of Tables	v
List of Figures.....	vi
List of Acronyms and Abbreviations	vii
1. Introduction.....	1
1.1 Background.....	1
1.2 Statement of the problem	2
1.3 Significance of the study.....	3
1.4 Research Questions	3
2. Literature Review.....	4
2.1 HIV/AIDS and HIV/AIDS Treatment	4
2.2 Magnitude of Virologic Non-suppression.....	4
2.3 Factors Associated with Non-suppression	5
2.3.1 Socio-demographic Factors.....	5
2.3.2 Clinical conditions (BMI, co morbidity, duration on ART, CD4...).....	5
2.3.3 ART related factors.....	6
2.3.4 Behavioral and social factors	7
2.4 Conceptual Framework.....	7
3. Objective of the Study.....	8
3.1 General Objective	8
3.2 Specific Objectives	8
4. Methods and Materials.....	9
4.1 Study Design.....	9
4.2 Study Period.....	9
4.3 Study Setting.....	9
4.4 Target or Reference Source Population	10
4.5 Study Population.....	10
4.6 Eligibility Criteria	10
Inclusion Criteria	10
Exclusion Criteria	11

4.7 Sample Size Determination.....	11
4.8 Sampling Technique	11
4.9 Study Instrument.....	13
4.10 Study Variables.....	13
4.11 Operational Definition	14
4.12 Data Collecting Method.....	15
4.13 Data Processing and Data Quality	15
4.14 Data Analysis.....	15
4.15 Ethical Consideration.....	16
4.16 Dissemination of Result.....	16
5. Result	17
5.1 Description of Study Participants	17
5.1.1 Description of Socio-demographic Characteristics of Study Participants	17
5.1.2 Description of Clinical and other Characteristics of Study Participants.....	18
5.2 Factors Associated with Virological Non suppression	19
5.2.1 Socio-demographic Factors Associated with Virological Non suppression	19
5.2.1 Clinical and other Factors Associated with Virological Non suppression.....	20
5.2.3 Independent Factors Associated with Virological Non suppression.....	21
6. Discussion.....	22
Limitations of the Study.....	23
7. Conclusions.....	24
8. Recommendations.....	24
References.....	25
Annexes	29
Annex 1: English version of consent form for patients.....	29
Annex 2: English version of written Questionnaire form	30
Annex 3: Amharic version of consent form for patients.....	32
Annex 4: Amharic version of written Questionnaire form	33

List of Tables

Table 1: Sample size estimation using Epi-info stat calc with different predictor factors...	11
Table 2: Socio-demographic characteristics of HIV +ve adolescents on HAART with and without viral suppression at public hospitals, Addis Ababa, Ethiopia, 2019.....	17
Table 3: Clinical characteristics of HIV +ve adolescents on HAART with and without viral suppression at public hospitals, Addis Ababa, Ethiopia, 2019.....	18
Table 4: Socio demographic factors associated with viral non-suppression among HIV +ve adolescents on HAART (n = 400) with and without viral suppression at public hospitals, Addis Ababa, Ethiopia, 2019.....	19
Table 5: Clinical factors associated with viral non-suppression among HIV +ve adolescents on HAART (n = 400) with and without viral suppression at public hospitals, Addis Ababa, Ethiopia, 2019.....	20
Table 6: Independent factors associated with virological non suppression among HIV +ve adolescents on HAART (n = 400) with and without viral suppression at public hospitals, Addis Ababa, Ethiopia, 2019.....	21

List of Figures

FIGURE 1: CONCEPTUAL FRAMEWORK SHOWING FACTORS ASSOCIATED WITH VIROLOGICAL NON SUPPRESSION	7
FIGURE 2: A SCHEMATIC PRESENTATION OF THE SAMPLING PROCEDURE	12

List of Acronyms and Abbreviations

AIDS	Acquired Immunodeficiency Syndrome
ART	Anti Retroviral Therapy
ARV	Antiretroviral
CD4	Cluster of Differentiation 4/glycoprotein found on surface of immune cells
CI	Confidence Interval
DBS	Dry Blood Spot
DU	Drug Use
HAART	Highly Active Antiretroviral Therapy
HIV	Human Immunodeficiency Virus
IRB	Institutional Review Board
MI	Mental Illness
PLHIV	People Living with HIV
RNA	Ribonucleic Acid
sdNVP	Single Dose Nevirapine
SPHMMC	Saint Paul's Hospital Millennium Medical College
TASH	Tikur Anbessa Specialized Hospital
TB	Tuberculosis
UNAIDS	United Nations Program on HIV/AIDS
VL	Viral Load
WHO	World Health Organization

1. Introduction

1.1 Background

Human immunodeficiency virus (HIV) is a leading cause of global burden of disease(1). At the end of 2017, the World Health Organization (WHO) estimated that about 36.9 million people worldwide were living with HIV, with Sub-Saharan Africa the most affected region in the world with 70% of the HIV burden(2). Ethiopia is one of the Sub-Saharan African countries with the highest numbers of people affected by the problem(3). In Ethiopia approximately 1.3 million people live with HIV and the estimated adult HIV prevalence is 0.9%(4). The number of people accessing antiretroviral therapy (ART) has gradually increased in the recent years(5). A key goal of ART is to suppress the replication of the virus. Suppressed viral replication facilitates restoration of the immune function and significantly reduces the risk of onward HIV transmission(6). Treatment with effective ART decreases morbidity and mortality among HIV positive individuals(7). Effective ART should lead to undetectable viral load within 6 months of initiation of therapy(8).

The WHO introduced viral load monitoring as a gold standard to follow up the treatment effectiveness in 2013(9). WHO recommends routine annual viral load monitoring for all patients on ART, as the most accurate available measure of treatment response(10). Establishment of the virological suppression status among patients enrolled on ART is important for timely detection of treatment failures, identification of patients in need of more intensive adherence support and minimizes development of drug resistance and unnecessary switch to expensive and limited ART regimen options(11).

Virological failure is classified as a plasma viral load above 1000 copies/ ml based on two consecutive viral load measurements after 3 months, with adherence support. If using dry blood spot (DBS) technology, a viral load above 300 copies/ml based on two consecutive viral load measurements after 3 months of treatment, with adherence support is also classified as virological failure(12).

Studies that have highlighted the factors associated with virological suppression in most developed countries and resource limited settings have used lower cut-offs to determine non-suppression. The thresholds used range from 300 to 500 copies/ml of blood(13). However, since several clinical and epidemiological studies have highlighted the risk of HIV transmission being very low when the viral load is lower than 1000 copies/ml, WHO recommends using 1000 copies/ ml as the threshold when using plasma and 500 copies/ ml for DBS(9).

In Ethiopia, viral load determination and guiding ART treatment with the gold standard test (viral load) has started recently because of resource limitation. Consequently, there is limited data on virologic non suppression and its associated risk factor. The national guidelines recommend that viral load testing should be done 6 months after initiating ART and thereafter annually for people who have achieved viral suppression. However, people with detectable viral loads undergo targeted intensified adherence support for 3 months followed by confirmatory viral load testing in order to differentiate poor adherence from treatment failure. Those with treatment failure as defined by two detectable viral load measurements above the threshold are switched to second-line ART(14).

1.2 Statement of the problem

Globally the number of patients receiving ART is significant. This means there is huge investment annually. The number of patients receiving ART in Ethiopia is also significant. In 2016, there were 720,000 people living with HIV and 27,104 newly diagnosed cases and 59% of them were enrolled in highly active antiretroviral therapy (HAART) program(15)(16). This implies significant cost for ART service delivery in finance, human resource, health infrastructure and time. All this investment in ART service delivery is to attain virologic suppression.

In 2014, a new global strategy was launched with the aim to end the AIDS epidemic by 2030. The Joint United Nations Programme on HIV/AIDS (UNAIDS) and partners set ambitious global targets for the year 2020. These include diagnosing 90% of all people living with HIV (PLWHIV), initiating antiretroviral treatment (ART) for 90% of those diagnosed with HIV infection and achieving an undetectable viral load in 90% of those on ART(17).

Ethiopia started to implement an ambitious plan launched by UNAIDS in 2014 known as “90–90-90”. This will focus to achieve, at least 73% of all HIV patients will be virally suppressed in 2020 and to end the AIDS epidemic by 2030. The 90–90-90 ambition plan intends to, by 2020; 90% infected individuals with HIV will be diagnosed, 90% diagnosed patients will be receiving ART drug and the viral load in 90% of patients on ART will be undetectable(18).

Even though there is huge investment in delivery of ART services globally and nationally virologic suppression is not yet attained. To achieve such a goal, research on the factors associated with virological non suppression is important because once these factors are identified intervention can be done to avert them. Nationally there were few studies done to identify possible factors hindering attainment of virologic suppression. The aim of this study is to identify factors associated with virological non-suppression. This information will be critical in identifying program interventions that can be further strengthened to optimize ART outcomes.

1.3 Significance of the study

There is increasing health cost in form of finance, human resource, infrastructure and time in delivering ART services to HIV patients in Ethiopia. All these investments are to attain viral suppression and restore immune function so that reducing HIV transmission and reduce the risk of opportunistic infections. Even though there is increasing investment in ART service viral suppression goal is not yet attained. Therefore this study tries to identify factors inhibiting attainment of viral suppression so that aversion of such factors facilitates viral suppression attainment. Additionally there was no such research done on public hospitals in Addis Ababa.

1.4 Research Questions

1. What are factors associated with virological non suppression among HIV +ve patients on HAART at public hospitals in Addis Ababa, Ethiopia?
2. What are possible recommendations to achieve virological suppression?

2. Literature Review

2.1 HIV/AIDS and HIV/AIDS Treatment

AIDS was first recognized in the United States in the summer of 1981. In 1983, human immunodeficiency virus (HIV) was isolated from a patient with lymphadenopathy, and by 1984 it was demonstrated clearly to be the causative agent of AIDS. Combination antiretroviral therapy (cART) was initiated in United States in 1995–1996; since marked declines were noted in the incidence of most AIDS-defining conditions in United States(19). Currently Highly Active Antiretroviral Treatment (HAART) is being utilized and it has dramatically reduced mortality and morbidity due to HIV.

The first evidence of HIV epidemic in Ethiopia was detected in 1984. Since then, AIDS has claimed the lives of millions and has left behind hundreds of thousands of orphans. Antiretroviral treatment began in 2003 and free ARV service was launched in January 2005 and public hospitals start providing free ARVs in March 2005. Expansion and strengthening ART care and treatment activities at regional, zonal, district (woreda) and kebele levels through targeted social mobilization and active community participation created an enabling environment to prevent and control spread of the epidemic. The process of task shifting: training of nurses and community health agents in prevention, treatment, care and support activities further strengthened community linkages and ensured availability of standard minimum packages of HIV/AIDS services at primary health care level. By 2017 there were more than 1100 health facilities providing HIV care and treatment service. ART coverage for adults (age 15+) has reached 76% but the coverage remains low (23.5%) for children (age <15) living with HIV(20).

2.2 Magnitude of Virologic Non-suppression

More than two thirds of all people living with HIV globally knew their HIV status in 2016. Among those who knew their HIV status, 77% were accessing antiretroviral therapy, and 82% of people on treatment had suppressed viral loads(15). In Ethiopia as of May 2018, 79 percent of PLHIV knew their status; 71 percent of eligible PLHIV are on ART and 87 percent of those on ART have attained viral suppression. However, viral load service coverage is 51 percent(21).

2.3 Factors Associated with Non-suppression

Studies from different settings have identified a wide range of factors that may be associated with virological non-suppression. These factors could be classified as socio-demographic factors, clinical factors, drug (ART) related, behavioral factors and viral factors (resistance to ART)

2.3.1 Socio-demographic Factors

Young age is associated with risk of virological non suppression(22). Children and adolescents on ART are more likely to have high viral loads(23). On the other hand, study done in Cambodia indicated that the likelihood of having viral non-suppression remained significantly lower among adolescents who were aged 17(24). Study done in Gondar, northwest Ethiopia showed that virological failure is higher among those aged < 35yrs(25) while study done in Tigray, northern Ethiopia indicated viral failure is associated with age < 40 years and male gender(26). On the contrary, study done in Denmark indicated that gender does not affect virological response to HAART(27).

Study done among HIV/AIDS patients on HAART attending University of Gondar Referral Hospital Northwest Ethiopia indicated level of education (no formal education and primary education) was a significant risk factor for treatment failure(28).

2.3.2 Clinical conditions (BMI, co morbidity, duration on ART, CD4...)

Higher odds of virological failure was observed among patients who had current body mass index(BMI) <16kg/m² compared with BMI >18.5kg/m², and BMI between 16 and 18.5kg/m² versus BMI >18.5kg/m²(29).

Virological non-suppression can also be caused by patient-related factors such as co-morbidities. Having active TB increased the odds of virological non-suppression (22). Study done in Addis Ababa on the virologic and immunologic outcome of HIV-1 infected patients with and without Tuberculosis showed clinical and latent Tb infections do not influence virologic and immunologic outcomes of ART in HIV patients(30). In another cohort study done on Tb co-infected patients in south west Ethiopia it showed that TB co-infection didn't adversely affect the immunologic outcomes, weight and hemoglobin responses even though it increased the risk of clinical failure nearly three times(31). Study done on HAART receipt and viral suppression among HIV-infected patients with co-occurring mental illness (MI) and illicit drug use (DU) in

USA showed that among those on HAART, concurrent MI/DU, and DU only, were also associated with a decreased odds of HIV-RNA suppression compared to those with neither. MI only was not associated with a statistically significant decrease in HAART receipt or viral suppression compared to those with neither. Co-occurring MI and DU is associated with lower HAART receipt and viral suppression compared to individuals with either MI or DU or neither(32).

Patients with WHO clinical staging 4 are more likely to be non-suppressed while those whose health status is evaluated by physicians on each clinic visit are less likely to experience virological failure(33).

The likelihood of having viral non-suppression remained significantly lower among adolescents had been on ART for more than 9 years, had most recent CD4 count of > 672 . On the other hand the likelihood of having viral non-suppression remained significantly higher for those on ART for < 6 years(28) among adolescents who had first viral load > 628 RNA copies/mL and among those who were receiving HIV care and treatment from an adult clinic(24). Another study done in the Tigray region of Northern Ethiopia showed that virological failure was associated with having CD4+ T-cells count < 250 cells/ μ L (26) while study done in Woldia and Desse, northeastern Ethiopia and study done in Gondar, northwest Ethiopia indicated that statistically higher odds of virological failure was observed among patients who had current CD4 T-cell count of < 200 mm³ compared with CD4 T-cell count of > 200 mm³(25)(29). Higher odds of virological failure was observed among patients who had taken ART for longer durations of 25–47 months and ≥ 48 months(25).

2.3.3 ART related factors

Second/third line ART regimens were protective against non-suppression(22). Drug and food interactions, drug-resistance (primary or transmitted) have also been associated with virological non-suppression. ARV regimen related factors such as drug adverse effects, suboptimal pharmacokinetics, suboptimal virological potency and food requirements are amongst other factors related to virological non-suppression(34). Study done among Ugandan children also indicated a NVP based first line regimen, prior exposure to sdNVP were associated with

treatment failure(35) while initial adult regimen D4T+ 3TC+ EFV, AZT +3TC+NVP, AZT+ 3TC+EFV and TDF+3TC+EFV were significantly protective for treatment failure(28).

2.3.4 Behavioral and social factors

Poor adherence/poor tolerability or non adherence increased the odds of virological non suppression(22)(26)(25)(29)(35). Drug intolerance is also the major cause of regimen discontinuations and hence virological failure(36). Alcohol consumption and non-disclosure increased the odds of virological failure(37). The possibility of having viral non suppression remained significantly lower among adolescents who had a relative as the main daily caregiver, and did not believe that there is a cure for AIDS compared to their reference group(24).

2.4 Conceptual Framework

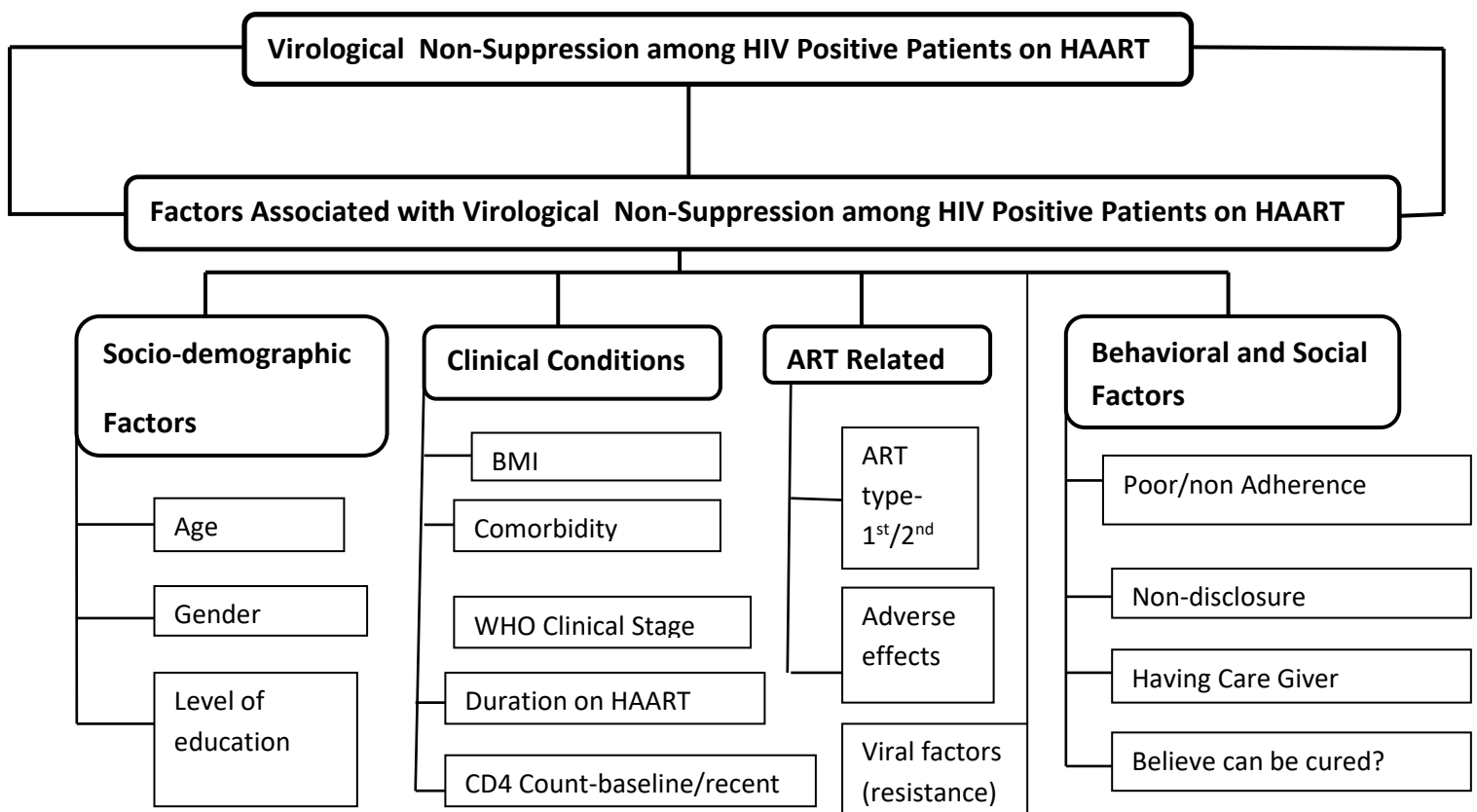


Figure 1: Conceptual framework showing factors associated with virological non suppression ((22)-(37)).

3. Objective of the Study

3.1 General Objective

- To determine factors associated with virological non-suppression among HIV + ve patients on HAART in public hospitals, Addis Ababa, Ethiopia

3.2 Specific Objectives

- To identify factors associated with virological non-suppression among HIV + ve patients on HAART in public hospitals, Addis Ababa, Ethiopia

4. Methods and Materials

4.1 Study Design

A 1:3 unmatched case-control study was used.

Cases: HIV +ve patients aged ≥ 15 yrs and on HAART for at least six months with two recent consecutive viral load test results ≥ 1000 copies/ml in a three month interval with enhanced adherence support

Controls: HIV +ve patients aged ≥ 15 yrs and on HAART for at least six months with two recent consecutive viral load test results < 1000 copies/ml

4.2 Study Period

The study was conducted from June 24, 2019 to July 19, 2019.

4.3 Study Setting

This study was conducted at three sampled public hospitals in Addis Ababa, Ethiopia. In Addis Ababa, there are 11 public hospitals and 18 private hospitals (overall 29 hospitals) all of them providing ART service. In addition, there are 98 health centers among which 78 provide ART services. There are also higher, medium and lower level clinics and some of which provide ART service. Overall there are 149 health facilities providing ART service and there are 94,426 clients on ART currently in Addis Ababa. ART service provision was started in Addis Ababa in 2003 and free ART started in 2005. Viral load service for patients on HAART is being given at 6 centers in the city.

This study was conducted in Zawditu Hospital, Saint Paul's Hospital and Yekatit 12 Hospital. Saint Paul's hospital and Zawditu hospital started ART service in 2003 while Yekatit 12 hospital started in 2006. The number of HIV + adolescents currently on HAART at Zawditu hospital, Saint Paul's hospital and Yekatit 12 hospital are 7477, 4655 and 2843 respectively. Until the time of this data collection, viral test was done for 7145 HAART adult patients at Zawditu, 4264 HAART adult patients at Saint Paul's and 2349 HAART adult patients at Yekatit 12 hospital. Among those with viral test result there are 571 virologically non suppressed and 6574 virologically suppressed adolescents at Zawditu hospital. At Saint Paul's hospital there are 472 virologically non suppressed and 3792 virologically suppressed adolescents among those with

viral test results. Similarly Yekatit 12 hospital currently has 382 virologically non suppressed and 1967 virologically suppressed adolescents among those with viral test result.

4.4 Target or Reference Source Population

For cases

All HIV +ve patients aged 15yrs and above and on HAART who have follow up at Addis Ababa public hospitals for at least six months and have two recent consecutive viral test results ≥ 1000 copies/ml within 3 months with enhanced adherence support.

For controls

- All HIV +ve patients aged 15yrs and above and on HAART who have follow up at Addis Ababa public hospitals for at least six months and have two recent consecutive viral test results < 1000 copies/ml.

4.5 Study Population

For cases:

- All HIV +ve patients aged ≥ 15 yrs and on HAART who were followed up for at least six months at selected public hospitals in Addis Ababa and have at least two recent consecutive viral test results ≥ 1000 copies/ml for plasma in a 3 month interval with enhanced adherence support

For controls:

- All HIV +ve patients aged ≥ 15 yrs and on HAART who were followed up for at least six months at selected public hospitals in Addis Ababa and have at least two recent consecutive viral test results < 1000 copies/ml for plasma

4.6 Eligibility Criteria

Inclusion Criteria

For both cases and controls:

- Outpatient department (OPD) patients on HAART
- Transfer-in clients in the last ≥ 6 months

Exclusion Criteria

For both cases and controls:

- Seriously ill HIV +ve patients on HAART
- Admitted HIV +ve patients on HAART
- Pregnant and lactating mothers

4.7 Sample Size Determination

Sample size was determined using Epi Info version 7.1 stat calc, by taking age < 35yrs as a predictor of virological non suppression(25) which gave sample size of 91 cases and 272 controls(25); P1=64.7%, P2=47.7%, 1:3 case to control ratio, 95% Confidence interval (CI), power of 80%, and it becomes 364 (91 cases and 273 controls). However to improve the power of the study **100 cases** and **300 controls** (overall 400) were included for this study.

Sample size calculated using other factors like current BMI < 16, current CD $\leq$ 200, duration on ART < 2yrs, and poor adherence, is shown in table 1 below:

Table 1: Sample size estimation using Epi-info stat calc with different predictor factors

SN	Factor	P1	P2	Number of Cases	Number of Controls	Comment (Source)
1	Age < 35yrs	64.7	47.7	91	272	(25)
2	Current BMI <16	17.7	6.5	71	212	(29)
5	Current CD4 $\leq$ 200	40.3	19.5	45	135	(29)
6	Duration on ART <2yrs	8.5	24.8	65	195	(25)
8	Poor adherence	42.2	12.3	19	56	(29)

4.8 Sampling Technique

The three hospitals (Saint Paul's Hospital, Zawditu hospital and Yekatit 12 hospital) were purposively sampled from public hospitals in Addis Ababa. St Paul's Hospital was selected among the hospitals under FMOH providing referral and teaching services. Zawditu hospital and Yekatit 12 hospital were selected from those under Addis Ababa Health Bureau for they are among hospitals with high ART clients. For cases, first proportional allocation of number of cases to respective hospitals was done based on the current number of HIV patients on ART with

virologic non suppression at each hospital (571, 472 and 382 at Zawditu, Saint Paul's and Yekatit 12 hospital respectively). Then the number of cases allocated for each hospital (40 for Zawditu Hospital, 33 for St Paul's Hospital, and 27 for Yekatit 12 Hospital) was divided to number of data collection days (20 working days). Data of cases allocated for each day for each hospital was collected using systematic random sampling among appointed virologically non suppressed cases for that specific day using appointment log book of each hospital. For each case three unmatched controls were taken using simple random sampling among virologically suppressed appointed controls for each specific day from respective hospitals. A schematic presentation of the sampling procedure is depicted in figure 1 below.

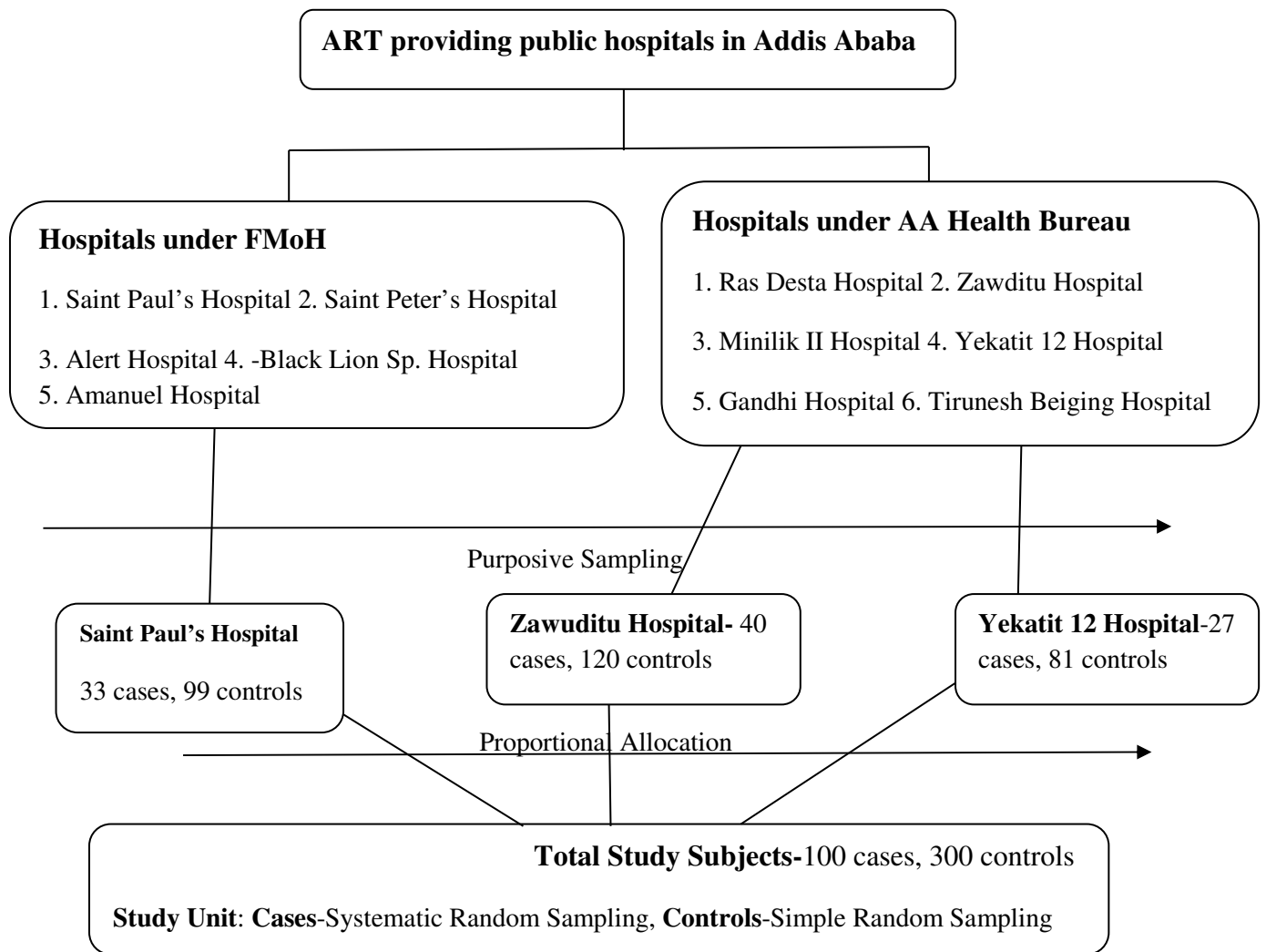


Figure 2: A schematic presentation of the sampling procedure

4.9 Study Instrument

A well structured questionnaire for data collection was developed from similar studies(26)(29) with some modifications in order to attain the objective of this study. It comprises socio demographic characteristics (age, sex, marital status, educational level, monthly income, current occupation, with whom one is living, presence or absence of family support, HIV status disclosure), and clinical data (weight, height, current and initial body mass index, initial WHO stage, baseline and recent CD4 count, initial and current ART regimen, initial and current viral load, co morbidity, duration on HAART, adherence status, previous documented adverse effects). It was prepared in English and was translated into local language (Amharic). In addition to this, chart or record or/and data review was done. Three Bsc Nurses (one for each hospital) working in that service area or ART clinic/OPD and one supervisor (health officer) was selected for data collection and training was given for all data collectors and supervisor for one day. Their recruitment was based on their willingness, experience and their department/OPD head recommendation. Nurses working in that service area were preferred over those working in other departments or facilities to avoid conflict of interest. Data collection took place at ART clinic/OPD of the three selected hospitals from June 24, 2019-July 19, 2019.

4.10 Study Variables

Dependent variables:

- ✓ Virologic non suppression (Yes/No)

Independent variables:

- ✓ Age (in years): different age groups, gender, marital status, occupation, income, Wt /Ht/BMI, level of education, Initial WHO clinical staging, CD4 cell count (baseline, recent), Initial viral load, current ART (1st line, 2nd/3rd line), initial ART regimen, co morbidity (having active TB, DM,,...), adherence, duration on ART, sero-status disclosure, having a relative as the main daily caregiver etc

4.11 Operational Definition

Virologic suppression:

- Having <1000 copies of HIV viral RNA/ml of blood plasma in two consecutive measurements in HIV +ve patients aged 15yrs and above and on HAART (1st line or 2nd /3rd line) for at least six months(12).

Virological non-suppression:

- Having ≥ 1000 copies of HIV viral RNA/ml of blood plasma in two consecutive measurements in 3 months interval with enhanced adherence support in HIV +ve patients aged 15yrs and above and on HAART (1st line or 2nd /3rd line) for at least six months(12).

Enhanced Adherence Support: Enhanced Adherence support is important for patients that have unsuppressed viral load. Components of enhanced adherence support (EAS) are(14):

- Review cognitive, behavioral, emotional and socio-economic barriers to adherence: treatment literacy, medications (dosage, timing, storage), side effects, discuss risk reduction (e.g. for substance abuse), motivation, mental health screening (screen for depression and other common mental problems using national mental health assessment tool), discuss patient's support systems
- Referrals and networking
- Assist patient to develop adherence plan to address the identified issues.

Medication adherence: the extent to which patients take medications as prescribed by their health care providers corresponds with agreed recommendations from a health care provider

- Good adherence: $\geq 95\%$ of doses are taken since started ART
- Fair adherence: 85-94% of the doses are taken since started ART
- Poor adherence: <85% of doses are taken since started ART

Tb Co infection: the presence current diagnosed Tb infection for which the patient is either on treatment (Anti Tb) or not.

Having family support: any support (psychological/emotional, physical, financial, or other) the patient is getting from his/her family member

Non-disclosure: means not telling someone that you are living with HIV

4.12 Data Collecting Method

A structured questionnaire with both open and closed ended questions was utilized to collect data from chart /ART data review and interview for patients. Data were collected by data collectors after they were given training on how to collect data by principal investigator for one day.

4.13 Data Processing and Data Quality

The data collected was entered to computer and cleaned on daily basis. Data entry was done by using Epi Info version 7.1 and exported to SPSS version 23 for analysis. The general data analysis was carried out after appropriate data entry task was completed. Any errors identified at this time were corrected after revision of the original data using the code numbers.

One supervisor and the principal investigator performed the supervision of data collection procedures on daily basis. They checked every completed questionnaire and gave onsite technical assistance to the data collectors. Anything, which was unclear and ambiguous, was clarified for data collectors. About 10% of the data were double entered by the clerk and the principal investigator to check consistency in putting data to SPSS.

4.14 Data Analysis

Analysis was done using SPSS version 23.0 to describe variables and assess associations. Descriptive statistics, including measures of central tendency and variation, was used to describe demographic, clinical, and medication-related characteristics of patients. Using binary logistic regression model, simple binary logistic regression analysis was carried out for all independent variables with an outcome variable. To consider more independent variables in the final analysis we used variables with a p-value of up to 0.2 in the simple binary logistic regression analysis, and finally multiple binary logistic regression analysis was carried out to identify the independent determinants of virological non suppression. The Hosmer–Lemeshow goodness-of-fit test for the model was also checked. Variables that have significant associations with virological non suppression were identified based on the odds ratio (OR) with a 95% CI and p-values <0.05. Lastly data were presented using text and tables.

4.15 Ethical Consideration

First ethical clearance from SPHMMC Institutional Review Board (IRB) and support letter to Addis Ababa city health bureau was written. After ethical clearance from SPHMMC and Addis Ababa city health bureau, support letter was written to Zawditu and Yekatit 12 hospitals. After communication with each hospital's clinical directors and ART clinic heads, individual consent from each study participants were filled after clear explanation about the purpose of the study. Anonymity of study subjects were maintained to insure confidentiality of information obtained. Privacy of respondents was also maintained during the interview.

4.16 Dissemination of Result

The study result will be disseminated to all institutions and partners being involved in HAART service delivery including those involved in this study for improving HAART service delivery. Additionally the result will be disseminated to SPHMMC department of public health in both soft and hard copies.

5. Result

5.1 Description of Study Participants

5.1.1 Description of Socio-demographic Characteristics of Study Participants

There were a total of 400 study participants (100 cases or virologically non-suppressed and 300 controls or virologically suppressed) in this study. Among the cases 56.0% were females while among the controls 72.7% were females. The mean age and standard deviation of cases was 37yrs and 10yrs respectively while the mean age and standard deviation of the controls was 43yrs and 10yrs respectively (See table 2 below).

Table 2: Socio-demographic characteristics of HIV +ve adolescents on HAART with and without viral suppression at public hospitals, Addis Ababa, Ethiopia, 2019

Socio-demographic characteristics	Category	Total (n=400) n(%)	Case (n=100) n (%)	Control (n=300) n (%)
Sex	Male	126 (31.5)	44 (44.0)	82 (27.3)
	Female	274 (68.5)	56 (56.0)	218 (72.7)
Age(Yr)	Mean	41.63	37	43
	Standard deviation	10.4	10	10
Age Category	<35 yrs	106 (26.5)	44 (44)	62 (20.7)
	≥35yrs	294 (73.5)	56 (56)	238 (79.3)
Marital Status	Single	85 (21.3)	32 (32)	53 (17.7)
	Married	168 (42)	39 (39)	129 (43)
	Divorced	65 (16.3)	16 (16)	49 (16.3)
	Widowed	82 (20.5)	13 (13)	69 (23)
Educational Level	Illiterate	28 (7)	6 (6)	22 (7.3)
	Read and write	24 (6)	1 (1)	23 (7.7)
	Elementary	137 (34.3)	33 (33)	104 (34.7)
	High School	134 (33.5)	40 (40)	94 (31.3)
	College or above	77 (19.3)	20 (20)	57 (19)
Occupation	Daily Laborer	29 (7.3)	7 (7)	22 (7.3)
	Farmer	6 (1.5)	1 (1)	5 (1.7)
	Govt Employee	85 (21.3)	14 (14)	71 (23.7)
	House Wife	45 (11.3)	7 (7)	38 (12.7)
	NGO Employee	22 (5.5)	4 (4)	18 (6)
	Private Business	63 (15.8)	16 (16)	47 (15.7)
	Retired	2 (0.5)	0 (0)	2 (0.7)
	Student	21 (5.3)	12 (12)	9 (3)
	Unemployed	52 (13)	16 (16)	36 (12)
Have Support	Yes	244 (61)	59 (59)	185 (61.7)
	No	156 (39)	41 (41)	115 (38.3)
Sero Status Disclosure	Yes	349 (87.3)	89 (89)	260 (86.7)
	No	51 (12.8)	11 (11)	40 (13.3)

5.1.2 Description of Clinical and other Characteristics of Study Participants

The mean duration on HAART of cases was 106 months (range 12 months to 189 months) while that of controls was 115 months (range from 18 months to 193 months). Among cases 31% had initial BMI below 18.5 while among controls 20.1% had initial BMI below 18.5. The percentage of cases with baseline CD4 <350/mm³ was 94% while that of the controls was 87%. On the other hand 99% of cases and 99.7% of controls were started on 1st ART initially. Considering initial VL, 95% of cases and 5.7% of controls had initial VL $\geq$ 1000 copies/ml (Table 3)

Table 3: Clinical characteristics of HIV +ve adolescents on HAART with and without viral suppression at public hospitals, Addis Ababa, Ethiopia, 2019

Clinical characteristics	Category	Total (n=400) n(%)	Case (n=100) n (%)	Control (n=300) n (%)
Initial BMI	<16	18 (4.5)	4 (4.0)	14 (4.7)
	16-18.49	73 (18.3)	27 (27.0)	46 (15.4)
	18.5-24.9	268 (67.2)	59 (59.0)	209 (69.9)
	25-29.9	34 (8.5)	8 (8.0)	26 (8.7)
	$\geq$ 30	6 (1.5)	2 (2.0)	4 (1.3)
Initial WHO stage	Stage I & II	127 (31.8)	27 (27.0)	100 (33.3)
	Stage III & IV	273 (68.3)	73 (73.0)	200 (66.7)
Baseline CD4	<350	355 (88.8)	94 (94.0)	261 (87.0)
	$\geq$ 350	45 (11.3)	6 (6.0)	39 (13.0)
Recent CD4	<350	128 (32.0)	74 (74.0)	54 (18.0)
	$\geq$ 350	272 (68.0)	26 (26.0)	246 (82.0)
Initial ART	1 st line	398 (99.5)	99 (99.0)	299 (99.7)
	2 nd /3 rd line	2 (0.5)	1 (1.0)	1 (0.3)
Current ART	1 st line	308 (77.0)	15 (15.0)	293 (97.7)
	2 nd /3 rd line	92 (23.0)	85 (85.0)	7 (2.3)
Initial VL	<1000	288 (72.0)	5 (5.0)	283 (94.3)
	$\geq$ 1000	112 (28.0)	95 (95.0)	17 (5.7)
Tb co infection	Yes	16 (4.0)	10 (10.0)	6 (2.0)
	No	384 (96.0)	90 (90.0)	294 (98.0)
Duration on HAART	<6yrs	93 (23.3)	27 (27.0)	66 (22.0)
	6-9yrs	68 (17.0)	24 (24.0)	44 (14.7)
	>9yrs	239 (59.8)	49 (49.0)	190 (63.3)
Adherence	Good	293 (73.3)	20 (20.0)	273 (91.0)
	Fair/poor	107 (26.8)	80 (80.0)	27 (9.0)
Documented Adverse Effects	Yes	23 (5.8)	8 (8.0)	15 (5.0)
	No	377 (94.3)	92 (92.0)	285 (95.0)

5.2 Factors Associated with Virological Non suppression

5.2.1 Socio-demographic Factors Associated with Virological Non suppression

Using simple binary logistic regression analysis, age <35yrs (COR=3.0, 95%CI 1.9-4.9), being male (COR=2.1, 95%CI 1.3-3.3), being married (COR=0.5, 95%CI 0.3-0.9) and being widowed (COR=0.3, 95%CI 0.2-0.7) were socio-demographic factors associated with virological non suppression (Table 4).

Table 4: Socio demographic factors associated with viral non-suppression among HIV +ve adolescents on HAART (n = 400) with and without viral suppression at public hospitals, Addis Ababa, Ethiopia, 2019

S N	Factor	Category	Case N=100	Control N=300	COR	CI	P value
1	Age category	<35yrs	44 (44)	62 (20.7)	3.0	1.9-4.9	<0.001
		≥35yrs	56 (56)	238 (79.3)	1.0		
2	Sex	Male	44 (44.0)	82 (27.3)	2.1	1.3-3.3	0.002
		Female	56 (56.0)	218 (72.7)	1.0		
3	Marital Status	Widowed	13 (13.0)	69 (23.0)	0.3	0.2-0.7	0.002
		Divorced	16 (16.0)	49 (16.3)	0.5	0.3-1.1	0.092
		Married	39 (39.0)	129 (43.0)	0.5	0.3-0.9	0.017
		Single	32 (32.0)	53 (17.7)	1.0		
4	Educational level	Illiterate	6 (6)	22 (7.3)	0.8	0.3-2.2	0.634
		Read & write	1 (1)	23 (7.7)	0.1	0.02-0.98	0.048
		Elementary	33 (33)	104 (34.7)	0.9	0.5-1.7	0.759
		High School	40 (40)	94 (31.3)	1.2	0.7-2.3	0.548
		College or above	20 (20)	57 (19)	1.0		
5	Family support	No	41 (41)	115 (38.3)	1.1	0.7-1.8	0.636
		Yes	59 (59)	185 (61.7)	1.0		
6	Sero status disclosure	No	11 (11)	40 (13.3)	0.8	0.4-1.6	0.545
		Yes	89 (89)	260 (86.7)	1.0		

5.2.1 Clinical and other Factors Associated with Virological Non suppression

Similarly using simple binary logistic regression analysis initial viral load ≥ 1000 copies/ml (COR=316.3, 95%CI 113.6-880.5), Tb co-infection (COR=5.4, 95%CI 1.9-15.4), 6-9yrs duration on HAART (COR=2.1, 95%CI 1.2-3.8), and poor/fair adherence (COR=40.4, 95%CI 21.6-75.9) were factors associated with virological non suppression (Table 5)

Table 5: Clinical factors associated with viral non-suppression among HIV +ve adolescents on HAART (n = 400) with and without viral suppression at public hospitals, Addis Ababa, Ethiopia, 2019

S/N	Factor	Category	Case N=100 N (%)	Control N=300 N (%)	COR	CI	P value
1	Initial BMI	<16	4 (4.0)	14 (4.7)	0.6	0.1-4.4	0.589
		16-18.49	27 (27.0)	46 (15.4)	1.2	0.2-6.8	0.858
		18.5-24.9	59 (59.0)	209 (69.9)	0.6	0.1-3.2	0.515
		25-29.9	8 (8.0)	26 (8.7)	0.6	0.1-4.0	0.611
		≥ 30	2 (2.0)	4 (1.3)	1.0		
2	Initial WHO stage	Stage III & IV	73 (73.0)	200 (66.7)	1.4	0.8-2.2	0.240
		Stage I & II	27 (27.0)	100 (33.3)	1.0		
3	Baseline CD4	<350	94 (94.0)	261 (87.0)	2.3	0.9-5.7	0.061
		≥ 350	6 (6.0)	39 (13.0)	1.0		
4	Initial ART	1 st line	99 (99.0)	299 (99.7)	0.3	0.02-5.34	0.436
		2 nd /3 rd line	1 (1.0)	1 (0.3)	1.0		
5	Initial VL	≥ 1000	95 (95.0)	17 (5.7)	316.3	113.6-880.5	<0.001
		<1000	5 (5.0)	283 (94.3)	1.0		
6	TB co infection	Yes	10 (10.0)	6 (2.0)	5.4	1.9-15.4	0.001
		No	90 (90.0)	294 (98.0)	1.0		
7	Duration on HAART	< 6yr	27 (27.0)	66 (22.0)	1.6	0.9-2.7	0.098
		6-9yr	24 (24.0)	44 (14.7)	2.1	1.2-3.8	0.013
		≥ 9 yr	49 (49.0)	190 (63.3)	1.0		
8	Adherence status	Poor/Fair	80 (80.0)	27 (9.0)	40.4	21.6-75.9	<0.001
		Good	20 (20.0)	273 (91.0)	1.0		
9	Documented Adverse effect	Yes	8 (8.0)	15 (5.0)	1.7	0.7-4.0	0.269
		No	92 (92.0)	285 (95.0)	1.0		

5.2.3 Independent Factors Associated with Virological Non suppression

Using multiple binary logistic regression analysis, independent factors associated with virologic non suppression among HIV +ve adolescents on HAART at public hospitals in Addis Ababa were age <35yrs (AOR=11.9, 95%CI 2.2-66.6), initial viral load $\geq$ 1000 copies/ml (AOR=324.0, 95%CI 66.2-1585.9) and poor/fair adherence (AOR=9.2, 95%CI 3.2-26.7) (Table 6).

Table 6: Independent factors associated with virological non suppression among HIV +ve adolescents on HAART (n = 400) with and without viral suppression at public hospitals, Addis Ababa, Ethiopia, 2019

S N	Factor	Category	Case N=100 N (%)	Control N=300 N (%)	COR (95% CI)	AOR (95% CI)	P value
1	Age category	<35yrs	44 (44)	62 (20.7)	3.0 (1.9-4.9)	11.9 (2.2-66.6)	0.005
		$\geq$ 35yrs	56 (56)	238 (79.3)	1.0		
2	Sex	Male	44 (44.0)	82 (27.3)	2.1 (1.3-3.3)	1.6 (0.5-5.2)	0.436
		Female	56 (56.0)	218 (72.7)	1.0	1.0	
3	Marital status	Widowed	13 (13.0)	69 (23.0)	0.3 (0.2-0.7)	0.4 (0.1-2.9)	0.382
		Divorced	16 (16.0)	49 (16.3)	0.5 (0.3-1.1)	0.5 (0.1-3.1)	0.454
		Married	39 (39.0)	129 (43.0)	0.5 (0.3-0.9)	0.8 (0.2-3.4)	0.789
		Single	32 (32.0)	53 (17.7)	1.0	1.0	
4	Initial VL	$\geq$ 1000	95 (95)	17 (5.7)	316.3(113.6-880.5)	324.0 (66.2-1585.9)	<0.001
		<1000	5 (5)	283 (94.3)	1.0	1.0	
5	TB co infection	Yes	10 (10.0)	6 (2.0)	5.4 (1.9-15.4)	6.2 (0.5-82.5)	0.166
		No	90 (90.0)	294 (98.0)	1.0		
6	Duration on HAART	< 6yr	27 (27.0)	66 (22.0)	1.6 (0.9-2.7)	0.7 (0.2-2.6)	0.586
		6-9yr	24 (24.0)	44 (14.7)	2.1 (1.2-3.8)	1.1 (0.3-3.8)	0.931
		$\geq$ 9yr	49 (49.0)	190 (63.3)	1.0		
7	Adherence	Poor/Fair	80 (80)	27 (9.0)	40.4 (21.6-75.9)	9.2 (3.2-26.7)	<0.001
		Good	20 (20)	273 (91.0)	1.0	1.0	

6. Discussion

In this study the mean age of cases was 37yrs (range 16 to 64yrs) and that of the controls was 43yrs (range 20 to 80yrs). The percentage of cases with baseline CD4 <350/mm³ was 94% while that of the controls was 87%. Considering initial VL, 95% of cases and 5.7% of controls had initial VL $\geq$ 1000 copies/ml. The study indicated that factors associated with virological non suppression among adolescents on HAART in public hospitals of Addis Ababa were younger age, initial viral load $\geq$ 1000 copies/ml and poor/fair adherence to HAART. This implies the importance of giving more attention to younger adolescents on HAART, those with initial viral load $\geq$ 1000 copies/ml and adherence support services to attain the goal of virological suppression as part of the three 90's.

Other factors which are found to be associated with virological non suppression in other studies like educational level, non disclosure, family support, initial BMI, initial WHO stage, baseline CD4 count, and presence of TB co infection were found not associated with virological non suppression in this study. This could be because of smaller sample size in this study to elicit such finding or it could be because of shorter data collection period or inadequate number of public hospitals sampled in this study which could affect representativeness of the study participants.

In this study, patients aged < 35yrs were 11.9 times more likely to develop virological non suppression than those aged $\geq$ 35yrs. This is supported by study done in Uganda(22), Gondar, northwest Ethiopia(25), and Tigray, northern Ethiopia(26). This might be due to differences in maturity or differences in lifestyle or workload and hence may forget to take medication properly. However, this needs further study.

The odds of virologic non suppression were 324 times more among those with initial viral load $\geq$ 1000 copies/ml than those with initial viral load <1000 copies/ml. This is supported by study done in Cambodia(24). This could be because of high initial viral load could affect early immunological recovery and hence virological suppression.

Patients with poor/fair adherence were 9.2 times likely to develop virologic non suppression than those patients with good adherence. This is compatible with study done in Harare city – Zimbabwe(37), Uganda(22), Kenya(38), Tigray, Northern Ethiopia(26), Woldia and Dessie, Northeast Ethiopia(29), and Gondar, northwest Ethiopia(25). This is because poor/fair adherence

results in low or suboptimal level of antiretroviral in the body which is not sufficient to suppress viral replication, hence leads to detection of HIV RNA level in the blood(39).

Limitations of the Study

- This study is limited to public hospitals which limited evaluation of factors associated with virological non suppression in private and nongovernmental health facilities.
- Incompleteness of patients' medical records
- Patients died at early phase of HAART because of different factors like OI/IRIS are difficult to be evaluated with this study

7. Conclusions

This study indicated that age <35yrs, initial viral load ≥ 1000 copies/ml and poor/fair adherence is factors that are significantly associated with virological non suppression.

8. Recommendations

Considering adherence, efforts should be strengthened to improve adherence to ART, which helps to suppress viral replication and load:

To Addis Ababa Health Bureau:

- Employ/assign adequate adherence supporters to ART service providing public hospitals in the city
- Train on adherence updates every adherence supporters assigned to each public hospital in the city

To Every Adherence supporters:

- Give adherence support to every HIV +ve adolescents especially those with virological non suppression at each visit.

To Every service provider at ART clinic:

- Give more attention to those <35yrs and on HAART and
- Those with initial viral load of ≥ 1000 copies/ml.

References

1. Haidong Wang, Mohsen Naghavi, Christine Allen, Ryan M Barber Z qar AB. Global , regional , and national life expectancy , all-cause mortality , and cause-specific mortality for 249 causes of death , 1980 – 2015 : a systematic analysis for the Global Burden of Disease Study 2015. 2017;1980–2015.
2. WHO fact sheet [Internet]. [cited 2018 Dec 10]. Available from: <http://www.who.int/mediacentre/factsheets/fs360/en/>
3. Ismail S, Hailemariam D. HIV/AIDS For the Ethiopian Health Center Team. 2002;
4. Federal Democratic Republic of Ethiopia/Central Statistical Agency. Ethiopian Demographic and Health Survey. 2016.
5. WHO. Antiretroviral therapy (ART) coverage among all age groups 2015 [Internet]. 2017. Available from: http://www.who.int/gho/hiv/epidemic_response/ART_text/en/.
6. Agwu AL, Fairlie L. Antiretroviral treatment, management challenges and outcomes in perinatally HIV-infected adolescents. 2013;1–13.
7. Bendavid E, Holmes C, Bhattacharya J. HIV Development Assistance and Adult Mortality in Africa. 2012;307(19):2060–7.
8. Soe AN, Tansuphasawadikul S, Phonrat B, Boonpok L, Tepsupa S, Japrasert C. Early Viral Suppression Predicting Long-term Treatment Success Among HIV Patients Commencing NNRTI-based Antiretroviral Therapy. 2010;2(2):33–7.
9. World Health Organization (WHO). Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection: recommendations for a public health approach. 2013;
10. World Health Organization (WHO). Health for the World's adolescents: a second chance in the second decade. 2014;
11. WHO. Technical Brief on HIV Viral Load Technologies. 2010;

12. World Health Organization (WHO). Global strategy for the surveillance and monitoring of HIV drug resistance. 2012;
13. James H McMahon, Julian H Elliott, Silvia Bertagnolio, Kubiak R JM. Viral suppression after 12 months of antiretroviral therapy in low and middle-income countries: a systematic review. 2013;377–85.
14. FDRE/MoH. National Guidelines for Comprehensive HIV Prevention, Care and Treatment, 2014. 2014.
15. Joint United Nations Programme on HIV/AIDS (UNAIDS). UNAIDS Data 2017. 2017;
16. Institute/EPHI E public health. HIV related estimates and projections for Ethiopia–2017. 2017;
17. United Nations Program on HIV/AIDS. Ambitious treatment targets: writing the final chapter of the AIDS epidemic. 2015;
18. Joint United Nations Programme on HIV/AIDS (UNAIDS). 90–90–90 An ambitious treatment target to help end the AIDS epidemic. 2014; Available from: <http://www.unaids.org/en/resources/documents/2017/90-90-90>
19. LONGO, FAUCI, KASPER, HAUSER, JAMESON L. Harrison’s Principles of Internal Medicine. 18th editi. 2012.
20. Ethiopian Federal Ministry of Health. National Guidelines For Comprehensive HIV Prevention , Care AND Treatment. 2017;
21. Federal HIV/AIDS Prevention and Control Office. HIV Prevention in Ethiopia National Road Map 2018-2020. (November 2018).
22. Bulage L, Ssewanyana I, Nankabirwa V, Nsubuga F, Kihembo C, Pande G, et al. Factors Associated with Virological Non- suppression among HIV-Positive Patients on Antiretroviral Therapy in Uganda , August 2014 – July 2015. 2017;1–11.
23. Jobanputra K, Parker LA, Azih C, Okello V, Maphalala G, Kershberger B et al. Factors associated with virological failure and suppression after enhanced adherence counselling, in children, adolescents and adults on antiretroviral therapy for HIV in Swaziland. 2015;

24. Chhim K, Mburu G, Tuot S, Sopha R, Khol V, Chhoun P, et al. Factors associated with viral non - suppression among adolescents living with HIV in Cambodia : a cross - sectional study. *AIDS Res Ther* [Internet]. 2018;1–10. Available from: <https://doi.org/10.1186/s12981-018-0205-z>
25. Belete Bayu, Amare Tariku, Abera Balcha Bult, Yohannes Ayanaw Habitu, Terefe Derso DFT. Determinants of virological failure among patients on highly active antiretroviral therapy in University of Gondar Referral Hospital , Northwest Ethiopia : a case – control study. 2017;153–9.
26. Hailu GG, Hagos DG, Hagos AK, Wasihun G, Dejene TA. Virological and immunological failure of HAART and associated risk factors among adults and adolescents in the Tigray region of Northern Ethiopia. 2018;30:1–17.
27. Thorsteinsson K, Ladelund S, Jensen-fangel S, Johansen IS, Katzenstein TL, Pedersen G, et al. Impact of gender on response to highly active antiretroviral therapy in HIV-1 infected patients : a nationwide population-based cohort study. 2012;
28. Ayele G, Tessema B, Amsalu A, Ferede G, Yismaw G. Prevalence and associated factors of treatment failure among HIV / AIDS patients on HAART attending University of Gondar Referral Hospital Northwest Ethiopia. 2018;1–13.
29. Ahmed M, Merga H, Jarso H. Predictors of virological treatment failure among adult HIV patients on first-line antiretroviral therapy in Woldia and Dessie hospitals , Northeast Ethiopia : a case-control study. 2019;1–7.
30. Kassa D, Gebremichael G, Alemayehu Y, Wolday D, Messele T, Baarle D Van. Virologic and immunologic outcome of HAART in Human Immunodeficiency Virus (HIV) -1 infected patients with and without tuberculosis (TB) and latent TB infection (LTBI) in Addis Ababa , Ethiopia. 2013;1–12.
31. Lenjisa JL, Wega SS, Lema TB, Ayana GA. Outcomes of highly active antiretroviral therapy and its predictors : a cohort study focusing on tuberculosis co - infection in South. *BMC Res Notes*. 2015;1–9.
32. Chander G, Himelhoch S, Fleishman JA, Hellinger J, Moore RD, Gebo KA. HAART receipt and viral suppression among HIV-infected patients with co-occurring mental illness and illicit drug use. 2009;21(5):655–63.
33. Huong DTM, Bannister W, Phong PT, Kirk O PL. Factors associated with HIV-1

- virological failure in an outpatient clinic for HIV-infected people in Haiphong, Vietnam. 2011;
34. AIDSInfor. Guidelines for the Use of Antiretroviral Agents in HIV-1-Infected Adults and Adolescents. Management of the Treatment-Experienced Patient. 2015;
 35. Sebunya R, Musiime V, Kitaka SB, Ndeezi G. Incidence and risk factors for first line anti retroviral treatment failure among Ugandan children attending an urban HIV clinic. 2013;1–10.
 36. d’Arminio Monforte A, Lepri AC, Rezza G, Pezzotti P, Antinori A, Phillips AN et al. Insights into the reasons for discontinuation of the first highly active antiretroviral therapy (HAART) regimen in a cohort of antiretroviral naive patients. 2010;
 37. Sithole Z, Mbizvo E, Chonzi P, Mungati M, Juru TP, Shambira G. Virological failure among adolescents on ART , Harare City , 2017- a case-control study. 2018;1–8.
 38. Hassan AS, Nabwera HM, Mwaringa SM, Obonyo CA, Sanders EJ, Wit TFR De, et al. HIV-1 virologic failure and acquired drug resistance among first-line antiretroviral experienced adults at a rural HIV clinic in coastal Kenya : a cross-sectional study. 2014;
 39. Nachega JB, Marconi VC, Zyl GU, Van GEM, Preiser W, Hong SY et al. HIV treatment adherence, drug resistance. Virologic Failure: Evolving Concepts. 2016;11(2):167–74.

Annexes

Annex 1: English version of consent form for patients

A) Information Sheet

Name of the hospital _____

Introduction: How are you? My name is _____. You are being asked to volunteer for participation in this research study. Before giving your consent, it is important that you get informed all about the research before the questions you will be asked

Objective of the study: The purpose of this study is to assess factors associated with virological non suppression among HIV +ve patients on HAART in public hospitals Addis Ababa. The study might be helpful for attainment viral suppression by identifying factors for non suppression and averting them by program implementers, service providers and patients in general.

Procedure: If you volunteer, you will be asked about your socio-demographic status, your clinical and follow up status to complete a two pages questionnaire that may take about 20-30 minutes. Some of the information will also be taken from your chart (folder).

Risks & benefits of being in the Study: We do not anticipate any risks for you in participating in this study other than taking your 20-30 minutes. Indirect benefits to participation are people who participate in this study may acquire additional knowledge about HIV AIDS, its treatment and follow up for better outcome.

Confidentiality and data Storage: The information you give me will be kept confidential and your name and address is not recorded in the interview to protect your confidentiality. The data collected will be stored besides the principal investigator in both hard copy and soft copy and access to data is limited to the principal investigator and those having legal authority for access.

Participation and withdrawal: You may refuse to participate in this research without penalty. If you choose to participate, you are free to answer or not answer for the questions which might be inconvenient for you or to withdraw at all without penalty. However, your information is very important to evaluate and improve the program.

Ethical Review: The ethics of this research were reviewed and approved by the Institutional Review Board (IRB) of St. Paul's Hospital Millennium Medical College. If you believe there has been any infringement of your rights as a research subject, you should contact the principal investigator or this hospital's clinical director either in person or via phone.

B) Participant Agreement (Written Consent form)

I have read/heard the information provided above. My signature below indicates my voluntary consent to participate in this research.

Signature of the participant _____ Name of person obtaining consent _____

Checked by: Supervisor's signature _____ Investigator's signature _____

Date _____

Annex 2: English version of written Questionnaire form

Section I: Socio demographic characteristics of patient questionnaire

Code	Questions	Coding Categories	Code for analysis
01	Sex of respondent	1. Male 2. Female	
02	Age of the participant	_____	
03	Marital Status	1. Single 2. Married 3. Divorced 4. Widowed	
04	What is your educational level?	1. Illiterate 2. Read & write 3. Elementary (1-8 grade) 4. High school (9-12 grade) 5. Diploma or above	
05	What is your total monthly income (in birr)?	_____	
06	What is your current occupation?	1. Governmental employee 2. Unemployed (Jobless) 3. NGO employee 4. House wife 5. Merchant 6. Daily laborer 7. Student 8. Other specify_____	
07	With whom you are living with?	1. Alone 2. Family 3. Parents 4. With his/her children 5. With related family 6. Other-----	
08	Do you have support from your family?	1. Yes 2. No	
09	If yes, for Q#10 what kind of support you are getting from your family?	1. Emotional/Psychological 2. Physical care and support 3. Financial 4. Counseling 5. Other_____	
10	HIV sero status disclosure	1. Yes 2. No	0. No 1. Yes

Section 2: Clinical follow up and others

Code	Questions	Coding Categories	Code for analysis
11	Wt (Kg) Ht (cm) Current BMI Initial BMI	 	
12	Initial WHO clinical staging	1. Stage I 2. Stage II 3. Stage II 4. Stage IV	
13	Baseline CD4 count	 	
14	Recent CD4 count	 	
15	Initial ART	1. First line 2. Second line 3. Other specify 	
16	Current ART	1. First line 2. Second line 3. Other specify 	
17	Initial viral load	 	
18	Recent viral load	 	
19	Comorbidity	1. Tb 2. DM 3. Cardiovascular 4. Other specify 	
20	Duration on HAART	 	
21	Current adherence status during the last month appointment	1. Good 2. Fair 3. Poor	
22	Ever on ART adherence status	1. Good 2. Fair 3. Poor	
23	Previous Documented Adverse Effects	1. Yes 2. No	0. No 1. Yes
24	Do you believe one can get cured of HIV?	1. Yes 2. No	0. No 1. Yes

Annex 3: Amharic version of consent form for patients

□) □□□□ □□□□

□□□□□□ □□ _____

□□□□: □□□□ □□? □□ _____ ገገገ _____ . □□□ □□□□□ □□□
□□□ □□□□□□ □□□□□ □□□□□ . □□□□□□□ □□□□□ □□□ □□ □□□□□□□ □□□□ □□□□
□□ □□□□ □□□ □□□□□ □□, □□ □□□□□ □□□□□□□ □□□□□ □□□ □□□□□□□□
□□□□□□□ □□□□□□ □□□□□□ □□□□□ □□.

□□□□ □□□□ □□□ □□□ □□□ □□□□□□□ □□□□□□ □□□ □□□□□□ □□□□□ / □□□□□□
□□□□□ □□ □□□□□ □□□□ □□□□ □□ □□□□□ □□□□□□□ □□□□□□ □□. □□□ □□□□□□
□□□□□□□□ □□□□ □□□□□ □□□□□□□□□□□□□, □□□□□□□ □□□□ □□ □□□□□□□
□□□□□□ □□□□□□ □□□□ □□□□□ □□□□ □□□ □□□ □□□□.

Procedure: □□□□□□□ □□□□ □□□, □□ □□□□□-□□-□□□□ □□□, □□ □□□□□ □□ □□□□□
□□□□ □□□□ □□□□□□□ □□□ □□□□□□□ 20-30 □□□□□ □□□ □□□□□. □□□□□□□
□□□ □□□□□□□ □□□□□ (□□□) □□.

□□□□ □□□ □□□□ □□□ □□ □□□□: □□□ □□□□ □□□ □□□□ □□

;;

(): -

-

.

-

,

.

.

,

.

-

:

-

(Institutional Review Board) (IRB)

.

,

.

B)

()

/

.

.

Date

□□□□□ □□□: □□□□ □□□□□ □□□ _____ □□ _____
 □□□□□□ □□□ _____ □□

Annex 4: Amharic version of written Questionnaire form

□□□ 1: □□□□□□□□ □□□□□□

01		1. 2.	
02		_____	
03		1. 2. 3. / 4. /	
04	?	1. 2. 3. 4.	
05	()	_____	
06	?	1. 2. () 3. 4. 5. 6. 7. 8. _____	
07		1. 2. 3. 4. / 5. 6. -----	
08	?	1. 2.	
09	10) (?	1. / 2. 3. 4. 5. _____	
10	/ A	1. 2.	

2:

.			
11	BMI BMI	_____	
12	WHO	1. I 2. II 3. III 4. IV	
13	CD4	_____	
14	CD4	_____	
15		1. 2. 3. _____	
16		1. 2. 3. _____	
17		_____	
18		_____	
19		1. 2. 3. 4. _____	
20		_____	
21		1.	

	□□□□□□ □□□□□□	2. □□□□□□□ □□□ 3. □□□	
22	□□□□□□ □□□□□□	1. □□ 2. □□□□□□□ □□□ 3. □□□	
23	□□□ □□ □□□□□□ □□□□□□□ □□□ □□□□	1. □□ 2. □□	
24	□□□ □□ □□ □□ □□ □ □□□□ □□□□ □□□ □□□□□?	1. □□ 2. □□	