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HEALTH

TIME TO VIRAL LOAD SUPPRESSION AND ITS ASSOCIATED FACTORS
IN COHORT OF PATIENTS TAKING ANTIRETROVIRAL TREATMENT IN
EAST SHEWA ZONE, OROMIYA, ETHIOPIA, 2018

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Abbreviations/acronym

μl	Microliter
3TC	Lamivudine
AIDS	Acquired Immuno- Deficiency Syndrome
AOR	Adjusted Odds Ratio
ART	Antiretroviral Therapy
ARV	Antiretroviral
ATT	Anti-Tuberculosis Treatment
AZT	Azidothymidine/Zidovudine
BCD ₄	Baseline Cluster of Differentiation 4
BMI	Body Mass Index
BPVL	Baseline Plasma Viral Load
BTB	Baseline Tuberculosis
CART	combination Antiretroviral Therapy
CD ₄	Cluster of Differentiation 4
CD ₈	Cluster of Differentiation 8
CDC	Center for Disease Control
CI	Confidence Interval
CMV	Cytomegalo Virus
d4T	Stavudine

EVF	Efavirenz
HAART	Highly Active Antiretroviral Therapy
HGB	Hemoglobin
HIV	Human Immuno-deficiency Virus
HR	Hazard Ratio
HSV	Herpes Simplex Virus
IQR	Interquartile Range
MAC	Mycobacterium Avium Complex
MTB	Mycobacterium Tuberculosis
MUAC	Mid Upper Arm Circumference
NVP	Nevirapine
OI	Opportunistic Infection
OR	Odds Ratio
P. jiroveci	Pneumocystis jirovecii
PI	Protease Inhibitors
PVL	Plasma Viral Load
RIF	Rifampin
RNA	Ribonucleic Acid
RT-PCR	Real Time Polymerase Chain Reaction
T. gondi	Toxoplasma gondii
TB	Tuberculosis

TLC	Total Lymphocyte Count
UNAIDS	Joint United Nations Programme on Human Immuno-Deficiency
Virus/ Acquired	Immuno- Deficiency Syndrome
VL	Viral Load
WHO	World Health Organization

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Summary

Background: Human immuno-deficiency virus (HIV) is a virus that causes Acquired Immuno-Deficiency Syndrome (AIDS). The key goal of ART is to achieve and maintain durable viral suppression. Thus, the most important use of the viral load is to monitor the effectiveness of therapy after initiation of ART. The main objective of the study was to determine the time for virological suppression and its associated factors among people living with HIV taking antiretroviral treatments in East shewa zone, Oromiya, Ethiopia.

Methods: The study was conducted in East Shewa zone, Oromiya, Ethiopia from August 2017 to January 2018. Patients diagnosed with human immunodeficiency virus presenting to the study health centers between October 3, 2011 and March 1, 2013 were included in the study given the following criteria: age 18 years or greater, eligible to start ART. All patients with baseline viral load measurement were included in the study. Interaction between explanatory variables with the response variable was analyzed by using cross tab features of SPSS, IBM Inc. Significance group comparison was done by Kaplan Meier log rank test. Cox proportional hazard model was used to select significant factors to the variability between groups. Data was collected by using structured questionnaires and interview. A total of ETB 81,120.00 was utilized to carry out the study.

Result: plasma viral load was suppressed below detection level in 72% of individuals taking different regimen of ART. The median HIV-1 plasma viral load in the cohort was log 5.3111 copies/ml. Survival curve difference were observed in category of marital status (p-value 0.023) and baseline CD4 values (p-value 0.023) whereas no significant difference were observed in Educational status (p-value 0.404), MUAC (p-value 0.407) BMI(p-value 0.335) and BTB(p-value 0.257). Estimated median time to PVL suppression was 181days (CI: 140.5-221.4) with the age group of 30-39years having minimum time to achieve suppression with 92 days (CI: 60.1-123.8) and the maximum time required to reach the level was age group between 50-59 years.

Conclusion: Estimated time to achieve PVL after taking ART was found to be 181 days. Factors affecting time to suppression level was marital status and baseline CD₄.

1. Introduction

1.1 Background

Human immuno-deficiency virus (HIV) is a virus spread through different body fluids that attacks the body's immune system, specifically the CD4 cells, often called T cells (1). Acquired immunodeficiency syndrome (AIDS) is a chronic, potentially life-threatening condition caused by the human immunodeficiency virus (HIV) (2). Globally, Mycobacterium tuberculosis is the most common opportunistic infection in HIV-infected individuals (3).

The world has committed to end the AIDS epidemic by 2030 as part of the sustainable Development goals (4). Momentum is now building towards a new narrative on HIV treatment and a new, final, ambitious, but achievable target: By 2020, 90% of all people living with HIV will know their HIV status, 90% of all people with diagnosed HIV infection will receive sustained antiretroviral therapy and 90% of all people receiving antiretroviral therapy will have viral suppression. When this three-part target is achieved, at least 73% of all people living with HIV worldwide will be virally suppressed – a two- to three-fold increase over current rough estimates of viral suppression. Modeling suggests that achieving these targets by 2020 will enable the world to end the AIDS epidemic by 2030, which in turn will generate profound health and economic benefits(5,6).

Viral load is a marker of response to ART. A patient's pre-ART viral load level and the magnitude of viral load decline after initiation of ART provide prognostic information about the probability of disease progression. The key goal of ART is to achieve and maintain durable viral suppression. Thus, the most important use of the viral load is to monitor the effectiveness of therapy after initiation of ART. Measurement of CD4 count is particularly useful before initiation of ART. The CD4 cell count provides information on the overall immune function of an HIV-infected patient. The measurement is critical in establishing thresholds for the initiation and discontinuation of opportunistic infection (OI) prophylaxis and in assessing the urgency to initiate ART(7).

Determinations of peripheral blood CD4+ T cell counts and measurements of the plasma levels of HIV RNA provide a powerful set of tools for determining prognosis and monitoring response to therapy. The CD4+ T cell count is the laboratory test generally accepted as the best indicator

of the immediate state of immunologic competence of the patient with HIV infection. Patients with CD4+ T cell counts $<200/\mu\text{L}$ are at high risk of disease from *P. jiroveci*, while patients with CD4+ T cell counts $<50/\mu\text{L}$ are at high risk of disease from CMV, mycobacteria of the *M. avium* complex (MAC), and/or *T. gondii*. The measurement of serum or plasma levels of HIV RNA has become an essential component in the monitoring of patients with HIV infection. The most commonly used technique is the RT-PCR assay. This assay generates data in the form of number of copies of HIV RNA per milliliter of serum or plasma and can reliably detect as few as 40 copies of HIV RNA per milliliter of plasma. Measurements of plasma HIV RNA levels should be made at the time of HIV diagnosis and every 3–6 months thereafter in the untreated patient. Following the initiation of therapy or any change in therapy, plasma HIV RNA levels should be monitored approximately every 4 weeks until the effectiveness of the therapeutic regimen is determined by the development of a new steady-state level of HIV RNA. In most instances of effective antiretroviral therapy the plasma level of HIV RNA will drop to <50 copies/mL within 6 months of the initiation of treatment. During therapy, levels of HIV RNA should be monitored every 3–6 months to evaluate the continuing effectiveness of therapy. Weight loss and malnutrition continue to be common problems among HIV-infected patients in such settings, even in the era of ART (7).

Viral load is the most important indicator of initial and sustained response to ART and should be measured in all HIV-infected patients at entry into care, at initiation of therapy, and on a regular basis thereafter (7). Viral load (HIV-RNA copies/mL of blood plasma) as a surrogate marker for disease progression was first developed enrolling male patients and is currently considered highly predictive of the clinical course of infection (8). A number of laboratory tests are important for initial evaluation of HIV-infected patients upon entry into care, and before and after initiation or modification of antiretroviral therapy (ART) to assess the virologic and immunologic efficacy of ART and to monitor for laboratory abnormalities that may be associated with antiretroviral (ARV) drugs. Two surrogate markers are routinely used to monitor HIV-infected patients: CD4 T lymphocyte cell count to assess immune function and plasma HIV RNA (viral load) to assess level of HIV viremia. (7). Plasma viral load is the primary predictor of HIV-1 transmission (9).

Center for Disease Control and prevention guidelines recommend that PVL and CD4 cell count be monitored at baseline, at four weeks after starting antiretroviral therapy and every three months thereafter (10).

Viral load monitoring is the gold standard practice in resource-rich countries for detecting treatment failure among people receiving ART. The 2013 WHO consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection recommend viral load testing as the preferred monitoring tool for diagnosing and confirming the failure of antiretroviral therapy. It recommend viral load testing six months after initiating ART and then annually for people receiving ART. Using plasma specimens for viral load testing is the preferred monitoring approach to determine viral failure at the threshold of 1000 copies/ml among people living with HIV (11).

Current WHO guidelines recommend antiretroviral therapy (ART) initiation in everyone living with HIV at any CD4 cell count (12). Because the quantity of HIV-1 in plasma is the primary predictor of HIV-1 transmission, consideration of plasma viral load in ART initiation guidelines is warranted (9).

Theoretical models and subsequent empiric data demonstrated that complete (or near complete) suppression of HIV replication is generally achieved with regimens containing three potent antiretroviral drugs and near perfect adherence. These regimen consisting of two nucleoside/nucleotide analogues plus either (1) a non-nucleoside reverse transcriptase inhibitor [NNRTI], or (2) a protease inhibitor boosted with $\leq 400\text{mg/day}$ ritonavir [boosted PI], or (3) a single protease inhibitor [non-boosted PI] (10). ART has dramatically reduced HIV-associated morbidity and mortality and has transformed HIV infection into a manageable chronic condition. It is highly effective at preventing HIV transmission (7). The primary clinical goal of ART is to inhibit viral replication and suppress plasma viral load (PVL) to undetectable levels. Studies have revealed that while a substantial proportion of individuals are able to achieve viral suppression with ART, at least one in ten patients will experience at least one episode of viral rebound (13).

Levels of virus vary greatly in most untreated patients, ranging from several thousand to a few million copies of HIV RNA per milliliter of plasma. Patients in whom viral plasma level is

suppressed to below detection by cART, (*combination antiretroviral therapy*), there is a continual low level of virus replication. Treatment with reverse transcriptase and protease inhibitors to HIV infected individuals resulted in a precipitous decline in the level of plasma viremia, which typically fell by well over 90% within 2 weeks. The number of CD4+ T cells in the blood also increased concurrently (3).

Earlier studies have shown that the total lymphocyte count (TLC), haemoglobin (HGB), body mass index (BMI), body weight and other simple laboratory and clinical markers predict mortality in HIV infected patients and thus can be used to identify patients at risk of dying (14).

The monitoring of ARV therapy using VL and genotypic resistance testing is essential to determining cases of treatment failure ; the quantification of VL serves as an indicator for whether ARV therapy leads to success or failure in HIV infected patients . To limit the emergence of resistance to ARV drugs, patients undergoing treatment for HIV should ideally undergo periodic virological monitoring, such as VL and genotypic resistance testing, to identify cases in which therapy has failed and to avoid the accumulation of drug resistance mutations(15).

1.2 Statement of the problem

According to UNAIDS 2016 report, 36.7 million people globally were living with HIV. 2.1 million people became newly infected with HIV, 1.1 million people died from AIDS-related illnesses , 78 million people have become infected with HIV since the start of the epidemic , 35 million people have died from AIDS-related illnesses since the start of the epidemic and 18.2 million people were accessing antiretroviral therapy the end of 2015. Sub-Saharan Africa remains most severely affected, with nearly 1 in every 25 adults (4.4%) living with HIV and accounting for nearly 70% of the people living with HIV worldwide. According to the 2016 HIV estimates, the national HIV prevalence in Ethiopia is 1.18 %, indicating the country has more than achieved the Millennium Development Goal 6 target of 2.5%(16).

Limited data are available on HIV viral suppression rates among men and women on antiretroviral therapy (ART) and factors associated with HIV RNA viral load (VL) suppression in Ethiopia(17). Studies identified different associated factors for viral suppression. Factors includes Non-ART use, younger age, and lack of awareness of HIV status (18), not receiving a single-tablet daily regimen, and immunological failure (17).

1.3. Significance of the study

The key goal of ART is to achieve and maintain durable viral suppression. Suppression of viral load leads to improvement of quality of life and reduction of HIV related morbidity and mortality. This study determined the duration at which the PVL becomes suppressed in a study of cohort of HIV patients. The degree of suppression of the PVL count indicates the predisposition to opportunistic infections and hence shorter-term risks of morbidity and progression to AIDS. The benefit of predicting the time of suppression in HIV patients was to determine the success of ART treatment, to determine the best possible time to shift ART regimens in case of toxicity and to suspect the possibility of drug resistance in patient taking ART drugs and to determine resistance of virus to drugs the patient is currently taking. Similar study was not done in East shoa zone, Oromiya, Ethiopia. The study will help ministry of health in making treatment formulation of treatment of OI in patients on ART in this study setting. It also is useful for patients who are taking ART to have an opportunity to shift in treatment regime and avoid unnecessary drug toxicity.

2. Literature Review

Decreases in viral load following initiation of ART are associated with reduced risk of progression to AIDS or death. Thus, viral load testing is an established surrogate marker for treatment response. The minimal change in viral load considered to be statistically significant (2 standard deviations) is a three-fold change (equivalent to a 0.5 log₁₀ copies/mL change). A study conducted in the United States shows that Fewer than one-third of HIV-infected individuals have suppressed viral loads, mostly resulting from undiagnosed HIV infection and failure to link or retain diagnosed patients in care (7).

After initiation of effective ART, viral load reduction to below limits of assay detection usually occurs within the first 12 to 24 weeks of therapy. Predictors of virologic success include: low baseline viremia, high potency of the ARV regimen, tolerability of the regimen, convenience of the regimen, excellent adherence to the regimen (7).

There was no evidence of association between undetectable final viral load and change of antiretroviral regimen. The analysis of the number of drugs per regimen revealed that 26% of the patients who received a double regimen had an undetectable final viral load; this percentage was 50% for patients treated with triple and quadruple regimens. patients treated with double regimen had odds of reaching an undetectable final viral load 67% lower than those receiving a triple regimen (19). In a study done in Brazil, among the patients retained in HIV care, 62% have suppressed virus (13). Of 139 HIV/AIDS patients exposed to the highly active antiretroviral therapy, virological failure was 12.2% (20).

The median HIV-1 viral loads of ART-untreated females and males were 42,200 copies/ml (8). The percentage of subjects who achieved virological suppression to <500 copies/mL differed by antiretroviral status. At 16 weeks, 93% of the antiretroviral-naive subjects with available data had achieved virological suppression, compared with 44% of antiretroviral-experienced subjects (21).

Antiretroviral treatment led to a mean reduction of 1.8 log₁₀ copies per ml with HAART, 1.2 log₁₀ copies per ml with RTI(reverse transcriptase inhibitor) combination therapy, and 0.4 log₁₀ copies per ml with monotherapy.

The proportion of patients reaching undetectable viremia was 12% percent for monotherapy, 41% for RTI combination therapy, and 63% for HAART. The percentage of participants reaching undetectable viremia (<400 HIV RNA copies per milliliter) during the observation period was higher for those undergoing HAART than those undergoing RTI monotherapy or combination therapy. Similarly, the proportion of participants with CD4 cell counts below $0.20 \times 10^9/L$ ($200/\mu L$) decreased more for those undergoing HAART (22).

Women with viral loads of <10,000 HIV-1 copies/mL and a CD4 T cell count >350 cells/mm³, having treatment with nelfinavir and a gestational age of >20 weeks at initiation of HAART showed a significantly shorter time to a VL of <50 copies/mL.(23).

In a study conducted , 21% individuals experienced viral rebound. Median time of suppression before rebound was 2 years. the probability of virologic failure was 0.85 after being suppressed for 12 months and it was 0.08 after 72 months being suppressed (p-value <0.01). (44)

Among low- and middle-income countries, Brazil, the Laos People's Democratic Republic, Malaysia, Mexico, Myanmar and the Republic of Moldova have achieved viral suppression for more than 80% of people receiving antiretroviral therapy (4).

Overall, 61.2% (95% CI: 56.4–66.1) of HIV-infected Kenyans aged 15–64 years had not achieved virological suppression. The base 10 median and mean VL was 4,633 copies/mL and 81,750 copies/mL respectively. Among 266 persons taking ART, 26.1% (95% CI: 20.0–32.1) had detectable viremia. Non-ART use, younger age, and lack of awareness of HIV status were independently associated with significantly higher odds of detectable viral load. persons aged 15–29 years had a significantly higher percentage of detectable viremia at 79.4% (95% CI: 72.4–86.5) than persons aged 30–64 years at 53.9% (95% CI: 48.4–59.5) ($p < 0.0001$) (18). Among 266 persons who were currently taking ART, significant differences in the proportion of detectable viremia across age groups were observed: 22.3% among persons aged 30–64 years compared with 46.5% among persons aged 15–29 years ($p < 0.0001$)(18). Patients between 16 and 24 years of age had odds of undetectable final viral loads 63% lower than those of age 45 or higher, but the statistical evidence was weak after adjustment for sex, viral load prior to adherence measurement, clinical stage, current immune status, duration of treatment, group of drugs, adherence and interval between two measurements of viral loads (OR=0.36; CI 95% 0.12-

1.09). There was no evidence of a difference in odds ratio of undetectable final viral loads for sex, clinical stage, current immune status and change of therapeutic regimens (19).

Regarding sex, in the ART-untreated group, females had consistently lower mean viral load than males for all groups >18 years old, although these differences were not statistically significant. For patients under ART, no sex-related differences were found except for those >55 years old where females had significantly lower mean viral loads. Female patients >55 years old showed statistically significant lower viral loads with respect to younger women. In addition, data from 31 pediatric patients (<11 years old) under ART were available for comparisons between sexes. It was observed a marked tendency to higher viral loads in girls than boys (median difference of 1.71 log₁₀ copies/mL), although it was not statistically significant (8).

HIV load was highest in subjects (25–29 years old) with incident HIV infection but increased with age in subjects with prevalent HIV infection (24). Older age was associated with lower levels of HIV-1 replication in this sample, independent of antiretroviral therapy usage, regimen adherence, and disease stage (25).

The mean of CD4+ T cells was significantly lower in old age compared to younger (107 ± 109 cell/mm³ vs. 178 ± 189 cell/mm³; $p < 0.01$), such as the mean CD4 percentage (9% vs. 14%; $p < 0.01$). The mean of CD8+ T cells at baseline was similar in old age and younger (757 ± 380 cell/mm³ vs. 818 ± 362) ($p = ns$). (26).

There were no significant differences found in the percentage of persons with detectable viremia by sex, marital status, widowhood, educational level, residence, region, and wealth index. Men and women who were taking ART had similar proportions of detectable viremia at 24.1% vs. 27.2%, respectively (18). The median age was 34.5 years and the median time on ART was 46 months. HIV viral suppression below 1000 copies/mL was 93%. Viral suppression among woman was not significantly different than among men (93.7% vs 92.9%; $P=0.59$) (17). Higher prevalence of undetectable viral load and lower levels of viral load have been associated with age above 45, female sex, CD4 counts higher than 200 cells/mm³, and lower levels of viral load at the beginning of treatment. Female patients, duration of treatment less than 6 months and CD4 cell counts of 200 cells/mm³ or higher gave a higher prevalence of undetectable final viral load (19).

Several reports have indicated that the HIV-1 viral load of infected individuals is lower in females than in males among the antiretroviral-untreated group, females had a significantly lower viral load than males (0.52 female/male median viral load ratio). When classified according to different ranges of CD4+T cell counts, females had consistently lower viral loads than males, although statistical significance was achieved only for the group in the range of 201-350. Patients with the lowest CD4 + T-cell counts showed similar viral loads for both sexes (8). When classified according to CD4+ T-cell count ranges, females showed a consistent tendency to lower viral loads than males, although a statistically significant difference between sexes was found only for the group within 201-350 cells/ml. Within this group the median viral load in males was 4-fold that observed in females (8).

Some study suggested the HIV load did not differ by sex, but, among subjects with prevalent HIV infection, it was higher in males than in females (24). Association was not observed in the effect of sex, clinical status, current immune status, and changes in treatment regimen (19).

HIV loads were found to be higher in men than in women, and concurrent infections with herpes simplex virus type 2 (HSV-2), tuberculosis, malaria, and helminthes have been associated with increased HIV. A high proportion (63.7%) of sero-conversions occurred in younger persons (15–29 years old), and the majority (54.7%) of subjects who seroconverted were female. When blood samples were obtained ~5 months after infection, the mean HIV load was 4.38 log₁₀ copies/ mL (median, 4.48 log₁₀ copies/mL) and was slightly higher in males than in females, but this difference was not statistically significant. Sixty-nine percent of females who seroconverted were >30 years old, compared with 56.9% of males (24).

Of the 1571 participants, 740 (47.1%) were women. Women had higher mean screening CD4 cell counts (average 15 cells higher, ($p < 0.001$), lower mean hemoglobin and creatinine clearance, a lower mean baseline HIV-1 viral load (4.85 log₁₀ vs. 5.05 log₁₀ copies/mL ($P < 0.001$)) and were less likely to have a prior AIDS diagnosis than men. The sex difference in viral load difference was related to CD4 cell count, however it was independent of country and persisted within the strata with CD4 < 200 cells/mm³. Women in resource limited settings have lower levels of plasma HIV-1 RNA and appear to present for enrollment into a clinical trials at an earlier stage of disease than men (28). The unadjusted mean HIV-1 RNA level was 5.05 log₁₀ copies/mL in men compared to 4.85 log₁₀ copies/mL in women ($p < 0.001$) (28).

Viral suppression among women (93.7%) was no different from among men (92.9%). The proportion of women and men who were married was not significantly different. Lower BMI, MUAC, and Hgb concentrations at ART initiation were strongly associated with a higher risk of death within 3 months. Among patients who survived 3 months after ART initiation, those with a decrease in weight, MUAC, or Hgb concentrations by 3 months had a higher risk of death during the first year. After 1 year, only a decrease in MUAC by 3 months after ART initiation was associated with a higher risk of death. Weight loss was associated with a higher risk of death across all levels of baseline BMI, with the highest risk observed among patients with BMI ,17 kg/m² (relative risk, 7.9; 95% confidence interval, 4.4–14.4) (29).

Patients with lower BMI, MUAC, or Hgb concentrations when they started ART were at a significantly higher risk of early mortality. Patients with a baseline MUAC of 20.0 cm had a 4.2-fold higher risk of early mortality compared with those with a baseline MUAC of >27 cm (95% CI, 3.3–5.2). The association between baseline MUAC and early mortality was attenuated, but remained statistically significant after further adjusting for baseline BMI (relative risk, 3.5; 95% CI, 2.6–4.7; MUAC ,20 vs >27 cm). Increased mortality was noted with weight loss, MUAC decreases, and Hgb decreases after 3 months of ART (29).

The median CD4 cell count at the start of ART was 105 cells /mm³ and increased significantly over 5 years of follow-up (30). The median baseline CD4 cell count for the entire cohort was 192cells/μl. Adjusted for CD4, MUAC and BMI, the HR for ART became 0.66 (0.42 to 1.03) (31). CD4+ cell count measured at last visit preceding HAART initiation (within 12 months prior) was fit both as a continuous variable and categorized (as <200 cells/mm³, 200–350, or >350); and nadir CD4+ cell count (defined as the lowest CD4+ cell count measured at any visit prior to HAART) (12). Median baseline CD4 count was 136 cells/mm³ (IQR 39–247), and was not significantly different between those with viral suppression (140 cells/mm³) and those with HIV viral load above 1000 copies/mL (112 cells/mm³) (P=0.19). Mean change in CD4 cell count while on ART was an increase of 304 cells/mm³, while 5.6% of those with both current and baseline CD4 tests available had a fall in CD4 cell count below baseline while on ART, meeting the definition for immunological treatment failure. Clinical treatment failure was experienced by 7.2% within the previous 12 months, but only 41 (3.3%) were WHO clinical stage III or IV at the time of the interview (17). Patients with initial CD4+ T cell count # 200 cells/mm³ had a

tendency to virologic failure; however, there was not any statistical significance. Studies conducted by Skowron et al demonstrated that T CD4+ cell count is a better predictor of viral suppression. However, in order to achieve viral load suppression to undetectable levels, it is necessary to have an optimal response of T CD4+ cell count in patients under antiretroviral therapy (20). A statistically significant negative correlation between viral load and CD4 + T-cell count was found in the ART-untreated group (8). CD4 count, haemoglobin, BMI, sex and clinical stage at enrolment were independent predictors of mortality (30).

Of 1428 continuous HAART users 39 (2.7%) were underweight, 521 (36.5%) normal weight, 441 (30.9%) overweight, and 427 (29.9%) obese at time of HAART initiation. being overweight or obese (vs. normal weight) was not independently associated with increased viral load level. Cumulative incidence of non-AIDS death was similar across all pre-HAART BMI categories. A report from the Women's Interagency HIV Study indicated that being overweight, obese, or morbidly obese was independently associated with higher CD4+ count, total lymphocyte count, and WBC counts compared to those of normal body mass index (BMI) (18.5–24.9 kg/m²) obesity (BMI ≥ 40 kg/m²) was associated with higher CD8+ counts. Studies of mortality risk conducted among HIV-infected populations even earlier in the HIV epidemic suggested protective associations of overweight against mortality (12).

Compared with patients with a baseline BMI between 18.5 and 22.9 kg/m², those with a BMI between 16.0 and 16.9 kg/m² had a 2.1-fold increased risk of early mortality (95% confidence interval, 1.7–2.5), and those with a BMI ,16.0 kg/m² had a 2.3-fold increased risk (95% CI, 2.0–2.7). In comparison, risk were 20% or 30% lower, respectively, in patients with a BMI between 23.0 and ,25.0 kg/m² (95% CI, .6–1.1) or between 25.0 and ,30.0 kg/m² (95% CI, .5–1.0). However, obesity (BMI, <30 kg/m²) at ART initiation was not associated with either a reduced or an increased risk of early mortality (29). Low body mass index (BMI≤18.5 kg/m²), low mid-upper-arm-circumference (MUAC≤250 mm), low CD4 cell count (≤350 cells/μl) were independent predictors of death (31). Median BMI at inclusion was 19.7 kg/m² (IQR 17.4–22.4, n=1057) and 256 mm (IQR 232–286, n=1064) for MUAC (31).

Significantly greater median increases in body weight (2.1 vs. 0.5 kg; p.045) occurred in subjects who achieved virological suppression (HIV-1 RNA load, <500 copies/mL) at week 16 than in subjects who did not (21).

Low body mass in adults (body mass index less than 18.5kg/m²), weight loss and wasting in children are all independent risk factors for HIV disease progression and mortality (32).

Body mass index (BMI) $\leq$ 18.5 kg/m² at baseline was associated with death in univariate analysis. Weight loss was seen in about a third of patients who survived up to the fourth week, and it was associated with increased death. Decline in TLC, HGB and BMI was associated with death in univariate analysis only (14).

Moderate to severe malnutrition was present in 16% of patients at the time of starting ART. It was found to be a significant independent predictor of death (hazard ratio (HR) 2.19, 95% confidence interval (CI) 1.29–3.73, $P < 0.004$ for those with BMI < 17 compared with those with BMI ≥ 18.5). Also Stage of disease (HR 2.47, 95% CI 1.20–5.07, $P < 0.014$ for those who were at stage C compared with those at stage A and the type of ART HR 0.50, 95% CI 0.27–0.93, $P < 0.03$ for highly active antiretroviral therapy (HAART) compared with non-HAART treatment. Malnutrition did not impair the magnitude of the increase in CD4 count at 6 or 12 months (14).

Tuberculosis co-infection was associated with virologic failure demonstrated with statistical significance, $P = 0.019$. Patients with a previous diagnosis of tuberculosis infection had 2.9 times great risk of virologic failure. In the logistic regression analysis the best model to explain the event of virological failure is the one that includes variables such as origin and infection by M. tuberculosis, yielding OR values of 3.2 and 3.8 respectively (20).

concurrent infections with herpes simplex virus type 2, tuberculosis, malaria, and helminthes have been associated with increased HIV viral load (24).

In bivariate analysis, younger age-group, lack of awareness of infection, no TB co-infection, not currently in HIV care, no current ART use, time in HIV care, lack of condom use at last sexual intercourse, and inconsistent condom use were significant predictors of detectable viral load at a p-value < 0.1 and were included in multivariable analysis. In multivariate analysis, non-ART use, younger age, and lack of awareness of HIV infection were associated with significantly higher odds of detectable VL. Persons who were not currently taking ART had almost 12 times as high

adjusted odds ratio (aOR) of having detectable VL as those who were currently taking ART (aOR 11.8, [95% CI:6.3–22.2]). Compared to persons aged 30–64 years, infected persons aged 15–29 years had more than three times the adjusted odds (aOR 3.3, [95% CI:2.1–5.3]), and persons unaware of their infection had more than twice the adjusted odds of having detectable VL (aOR 2.2, [95% CI: 1.1–4.4]) (18).

unsuppressed HIV VL was independently associated with lower CD4 cell count, social isolation, high stigma, not receiving a single-tablet daily regimen, multiple late appointments in past year, and immunological failure (17).

The median time to undetectable VL after initiation of treatment was 60 days (12–168 days). Only baseline VL <10,000 copies/mL showed an independent association with time to viral suppression with a mean time to reach a VL <50 HIV-1 copies/mL of 49 days (95% CI 44–53). No difference in time to undetectable VL was found between protease inhibitor and non-nucleoside reverse transcriptase inhibitor-based regimens. Integrase inhibitors were not part of any treatment regimen. A multivariable Cox proportional hazards analysis using the above mentioned variables showed an independent association only of baseline VL <10,000 copies/mL with a shorter time to viral suppression (23).

Undetectable final viral load occurred in 48% of the patients. The crude odds were lower for age 16–24 years and use of Nucleoside Analog Reverse Transcriptase Inhibitors only, but these effects were not significant in the multivariate model. There was no evidence of effect of sex, clinical status, current immune status, and changes in treatment regimen. Treatment adherence gave the largest effect. Motivational interventions directed at adherence may improve treatment effectiveness. (19). The first 4 to 6 weeks of treatment are marked by a trend of reduction in viremia of at least 1.0 log₁₀, which represents 90% of the initial viremia and, in the next 12 to 24 weeks the viremia is expected to be undetectable or 99% lower than its initial level or from 5,000–10,000 copies/ml (19).

Patients who had a VL taken at month 3 versus at month 6 were 22% less likely to experience virological failure and 27% less likely to be switched to a second line regimen. For each additional month of delay in taking the first viral load (between 2.5 and 9 months) the risk of virological failure increased by 9% and the risk of treatment switching increased by 14% (33).

In one study the 277 participants contributed 995 person-years of follow-up with a median follow-up time of 32 months (IQR: 6 – 64) per participant. One hundred twenty-five participants (45.1%) experienced at least one instance of viral rebound over follow-up, equal to a crude incidence of 12.6% (95% CI: 10.5–15.0) (13).

For incident HIV infection, the mean time from seroconversion to measurement of HIV load was 5 months, assuming a uniform distribution of seroconversions during the 10-month follow-up intervals (24).

Of the 1305 individuals who achieved an initial virologic response, 274 (21%) subsequently experienced viral rebound. The median time of suppression before rebound in these 274 individuals was 2.0 years (10).

3. Objective

3.1 General Objective

- To determine the time to virological suppression and its associated factors among people living with HIV taking antiretroviral treatments in East shewa zone, Oromiya, Ethiopia, 2017.

3.2 Specific Objective

- To describe the distribution of time to PVL suppression of HIV patients
- To determine factors affecting the time at which HIV-1 viral load level becomes suppressed below detection level
- To provide recommendation based on findings to ministry of health

4. Methods and Materials

4.1 Study area

The study was conducted in East Shewa zone, Oromiya region, Ethiopia. The study area covers population of approximately 600,000 residents. Location of the study includes Adama and Geda health centers from Adama town and Dhera, Wolenchiti and Modjo health centers from area surrounding Adama town in East shewa zone. (1)

East Shewa is one of the Zones of the Ethiopian Region of Oromia. This zone is bordered on the south by the West Arsi Zone, on the southwest by the Southern Nations, Nationalities and Peoples Region, on the west by South west Shewa and Oromia Special Zone. It Surrounds Addis Ababa, on the northwest by Gelan town, on the north by the Amhara Region, on the northeast by the Afar Region, and on the southeast by Arsi(Assela). The number of health facility in the zone includes 4 Hospitals, 59 health centers and 291 health posts. In terms of coverage, the zone has 100% coverage in Hospital, health center and health post. ART site in the zone includes 4 hospitals and 12 health centers. The number of people currently taking ART in East shewa zone is 5021(34).

4.2 Study design and period: Retrospective cohort study was conducted from August 1, 2017 to January 30, 2018 on secondary data.

4.3 Source population: The source population were all people with confirmed HIV positive status in East Shewa Zone, Oromiya region Ethiopia.

4.4 Study population: Patients who have started ART since inclusion constitute the study population for the current study, with follow-up data collected until data abstraction on December 31, 2013.

4.5 Sample size determination and sampling

All 243 study participants with base line viral load measurement was included from the study

“High Rates of Virological Suppression in a Cohort of Human Immunodeficiency Virus-Positive Adults Receiving Antiretroviral Therapy in Ethiopian Health Centers Irrespective of Concomitant Tuberculosis”.

4.6 Study variables

Response variable: Time of viral load suppression level

Independent variable: Base line Plasma Viral Load(BPVL), PVL at 3rd month, 6th month, 12th month and 18th month, Age, sex, marital status, occupation, educational level, height, weight, Mid Upper Arm Circumference(MUAC), baseline CD₄(BCD₄) and baseline Tuberculosis(BTB).

4.7 Data collection tools & procedures

Data was extracted from a long-running community-recruited prospective cohort study of patients of HIV taking ART in East shewa zone, Oromiya Ethiopia. The study has been ongoing for the last eight years. Original article of the study can be found from Reepalu et al. Demographic and clinical data, including physical examination details, were collected at the start of the study by Reepalu et al. Data was collected by structured and pretested questionnaire. Interview was also used to collect data from patients. After informed consent, data was collected and checked for completeness.

4.8 Eligibility criteria

4.8.1. Inclusion criteria

Human immunodeficiency virus(HIV)-positive patients presenting to the study health centers between October 3, 2011 and March 1, 2013 were eligible for inclusion given the following criteria met:

- age 18 years or greater
- Residency in the catchment area of any of the study sites
- Patients with current or previous ART,

4.8.2. Exclusion criteria

- Age less than 18 years old, with current or previous ART
- Patients on ATT for more than 2 weeks before inclusion

4.10 Standard definitions

Baseline VL: the last known VL before HAART initiation.

Viral suppression: refers to a viral load below the detection threshold using viral assays.

Treatment failure: the current WHO virological criterion for treatment failure is when there are 1000 copies of virus per ml or more.

Viral rebound: the first of at least 2 consecutive viral loads >400 copies/ mL following initial viral suppression.

Duration of suppression at any month was defined as the number of prior consecutive months of viral suppression.

Virologic failure: as a confirmed viral load >200 copies/mL—a threshold that eliminates most cases of apparent viremia caused by viral load blips or assay variability.

Clinical failure: any WHO stage III or IV illness in the past 12 months.

Immunological failure: current CD4 cell count less than CD4 cell count at time of ART initiation.

4.11 Data Quality: Training was given for two data clerks on data management of secondary data obtained from previous study. Pretest of data collection tools was done in the study areas before actual data collection procedure. Double entry of data made by using EPIINFO 7 to minimize error in data management and was analyzed by SPSS version 21.

4.12 Data Analysis

Once data is collected, it was analyzed **descriptively** to determine the demographic characteristics and distribution of time to PVL. **Bivariate** analysis was used to identify variables, which has association with dependent variable. Time to undetectable viral load level was calculated by using **Kaplan–Meier** to estimate the distribution of PVL in time, and differences between the survival curves was evaluated with the use of the **log-rank test**, which is useful for comparing potentially unequal follow up times of study participants. **Cox proportional-hazards** regression analysis used to relate covariates with response variable with 95% confidence intervals.

4.13 Ethical considerations

Ethical approval was obtained from Saint Paul's Hospital Millennium Medical college public health department ethical review committee. Then the approval letter was forwarded to Oromiya regional health beuro. Finally, the approval letter from regional health bureau submitted to Adama regional laboratory where the actual study was done. Study participants provided written

informed consent. Informed consent were received from illiterate study participants in the previous study (35).

5. Result

Study participant Characteristics

Study participants were recruited from Adama , Dhera, Geda, Modjo and Wolenchiti health centers taking ART and selected according to eligibility criteria. The minimum age included in the study was 18 years and the maximum age was 69 years old. The mean, median and mode of participant age was 34, 32 and 30 years of age respectively. Forty five percent of the participants age was between 20-29 years old and minimum category was observed in <20 years old with 1.6 percent. Sex distribution of the study participant was 41% male and 59% female participants. most of the study participants (41%) was married but widowed participant represent only 10 % of the participant. With regard to baseline viral load in which the measurement was taken when the study participants enrolled in to the study, 13% of them were with plasma viral load less than 10,000 copies/ μ l. plasma viral load was suppressed in 72% of individuals taking different regimen of ART treatment. The median HIV-1 plasma viral load in the untreated cohort was log 5.3111 copies/ml. Nine percent of participant complete higher education while 36% of them were illiterate. Study participants nutritional status was also assessed by the study. Six participants (2.46%) were classified as having acute malnutrition while 71(29.2%) Participants classified as having moderate malnutrition and the rest 166 (68.3%) were classified as normal. Baseline CD₄ count was determined at the beginning of the study. Based on the data 140(57.6%) of the participants have BCD₄ count of <200 cells/ μ l, 77(31.7%) have BCD₄ count 200-350 cells/ μ l and 26(10.7%) have BCD₄ count of >350 cells/ μ l. Tuberculosis disease screened among participants before enrollment and 189(77.8%) were positive for MTB by AFB light microscopy smearing and culture (MGIT and LJ). Viral rebound was seen in 16.5% of study participant. The Proportion of patients having PVL suppressed after taking ART was 72.4%.

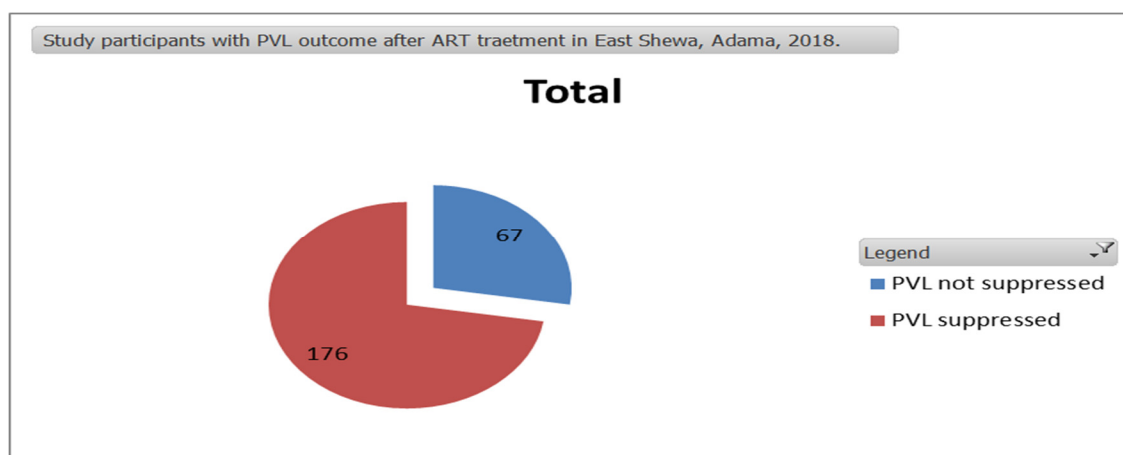


Figure 1. Proportion of HIV patients taking ART with PVL suppression level, East Shewa Zone, Oromiya , Ethiopia, 2018.

Majority of the study participant age group was between 20-29 years old and age group <20 years old included in the study was only 1.6%. Female participants accounts for almost 60% of the study participant.

Table 1. Socio-demographic description of study participants, East Shewa Zone, Oromiya , Ethiopia, 2018

Variables		Number(percent)
Age	<20 years	4(1.6)
	20-29 years	109(44.9)
	30-39 years	91(37.4)
	40-49 years	29(11.9)
	50-59 years	7(2.9)
	≥60 years	3(1.2)
sex	Male	99(40.7)
	Female	144(59.3)
residency	Adama	68(28)
	Dhera	19(7.8)
	Geda	32(13.2)
	Modjo	70(28.8)
	Wolenchiti	54(22.2)
Marital status	Single	56(23.0)
	Married	112(46.1)
	Divorse	50(20.6)
	Widowed	25(10.3)
BPVL	<10,000 copies/μl	31(13)

	$\geq 10,000$ copies/ μl	212(87)
Event occurred	Yes	176(72.4)
	No	67(27.6)
Education status	Illiterate	88(36.2)
	<6 grade	65(26.7)
	06-12 grade	81(33.3)
	Higher education	9(3.7)
BMI	<18.5 Kg/m ²	85(34.97)
	≥ 18.5 -24.9 Kg/m ²	146(60.08)
	25-29.9 Kg/m ²	11(4.52)
	>30 Kg/m ²	1(0.41)
MUAC	<18 cm	6(2.46)
	18-21 cm	71(29.2)
	>21 cm	166(68.3)
BCD ₄	<200 cells/ μl	140(57.6)
	200-350 cells/ μl	77(31.7)
	>350 cells/ μl	26(10.7)
BTB	Positive	189(77.8)
	Negative	54(22.2)
Treatment regimen	d4T, 3TC, NVP	1(0.4)
	d4t, 3TC, EFV	5(2.1)
	AZT, 3TC, NVP	13(5.3)
	AZT, 3TC, EFV	13(5.3)
	TDF, 3TC, NVP	17(7.0)
	TDF, 3TC, EFV	168(69.1)
Occupation	Outdoor	170(70)
	Indoor)	72(30)
Viral rebound	Yes	40(16.5)
	No	203(83.5)

Bivariate analysis

Base line PVL status of a patient did not showed significant interaction with event of interest with χ^2 value 2.33(p-value .127). Other variables which did not show up includes age of the

patient χ^2 value of 4.44 (p-value .488), Marital status χ^2 value of 6.75 (p-value .081), occupation χ^2 value of .383 (p-value .826), education status χ^2 value of 1.13 (p-value .770), MUAC χ^2 value of .253 (p-value .881), BTB with χ^2 value of 1.15 (p-value .283).

Significant interaction or association with Plasma viral load suppression were observed in sex χ^2 value of 5.06 (p-value .024), BMI with 0.003, BCD₄, χ^2 value of 10.98 (p-value .004) and ART Treatment regimen with χ^2 value of 14.23 (p-value .0027).

Table 2. Bivariate crude estimates, analysis of study participants, East Shewa Zone, Oromiya , Ethiopia, 2018.

Variables	Category	Count/ percent	p- χ^2 value	Sign.
BPVL	<10000 copies/ μ l	31(13)	2.33	.127
	>10000 copies/ μ l	212(87)		
Age	20 years	4(1.6)	4.44	.488
	20-29 years	109(44.9)		
	30-39 years	91(37.4)		
	40-49 years	29(11.9)		
	50-59 years	7(2.9)		
	≥ 60 years	3(1.2)		
sex	Male	99(40.7)	5.06	.024
	Female	144(59.3)		
Marital status	Single	56(23.0)	6.75	.081
	Married	112(46.1)		
	Divorce	50(20.6)		
	Widowed	25(10.3)		
occupation	Outdoor	170(70)	.383	.826
	Indoor	72(30)		
Educational status	Illiterate	88(36.2)	1.13	.770
	<6 grade	65(26.7)		
	6-12 grade	81(33.3)		
	Higher education	9(3.7)		
BMI	≤ 18.5 kg/m ²	87(35.8)	8.98	0.003
	>18.5 kg/m ²	156(64.2)		
MUAC	≤ 23 cm	≥ 23 cm	.253	.881
	23.1-24.9 cm	23.1-24.9 cm		
	≥ 25 cm	≥ 25 cm		
BCD ₄	<200 cells / μ l	140(57.6)	10.98	.004
	200-350 cells / μ l	77(31.7)		
	>350 cells / μ l	26(10.7)		
BTB	Positive	189(77.8)	1.15	.283
	Negative	54(22.2)		
Treatment regimen	d4T, 3TC, NVP	1(0.4)	14.23	0.027

d4t, 3TC, EFV	5(2.1)
AZT, 3TC, NVP	13(5.3)
AZT, 3TC, EFV	13(5.3)
TDF, 3TC, NVP	17(7.0)
TDF, 3TC, EFV	168(69.1)

Laboratory analysis

All laboratory analyses, except TB cultures, were performed at Adama Regional Laboratory. CD4 cell counts were analyzed using BD FACSCalibur cytometer (Becton Dickinson, San Jose, CA). Sputum and FNA samples were analyzed with direct smear microscopy using Ziehl-Neelsen staining and Xpert MTB/RIF (Cepheid, Sunnyvale, CA) for polymerase chain reaction. Liquid cultures for TB were performed at International Clinical Laboratories, Addis Ababa, using a BACTEC MGIT 960 (BD Diagnostics, Franklin Lakes, NJ). Plasma HIV-RNA levels were determined using Abbott Real- Time HIV-1 assay (Abbott Molecular Inc., Des Plaines, IL) with a detection limit of 40 copies/ml. External quality assurance of the regional laboratory is regularly performed by the Center for Disease Control and Prevention (Atlanta, GA).

Comparison between different categories for survival

Survival distribution for different age group reveals that there was no significant difference between different age group in terms of the time to reach suppressed plasma viral load with log rank test score of χ^2 value 0.860. Estimated median time to PVL suppression was **181days** (CI: 140.5-221.4) with the age group of 30-39years having minimum time to achieve suppression with 92 days (CI: 60.1-123.8) and the maximum time required to reach the level was age group between 50-59 years.

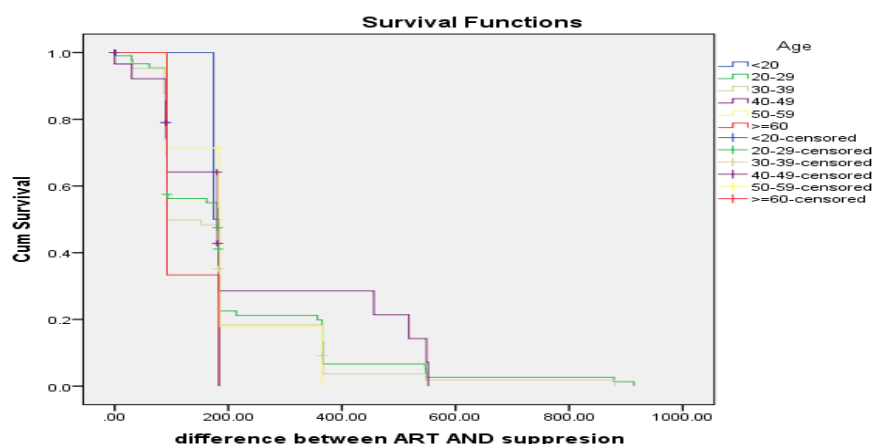


Figure 2. Survival curve between different age groups of study participants in East Shewa Zone, Oromiya , Ethiopia, 2018.

Survival distribution of study participant by sex category indicated that there were no significant difference between male and female in terms of time to reach viral suppression level in the plasma. In the log rank test was, χ^2 value was 3.499 with p-value of 0.061.

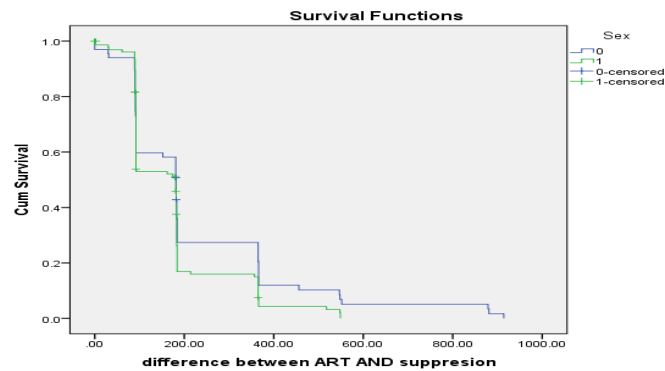


Figure 3. Survival curve between different age groups of study participants in East Shewa Zone, Oromiya , Ethiopia, 2018.

Significantly different survival distribution curve was observed between different categories of marriage in the study participants. The maximum median time for PVL suppression was observed in unmarried participants with 183 days (CI: 181.7-184.315). The minimum median time registered in divorced participant category with estimated median time of 92 days (CI: 91.06-92.93).

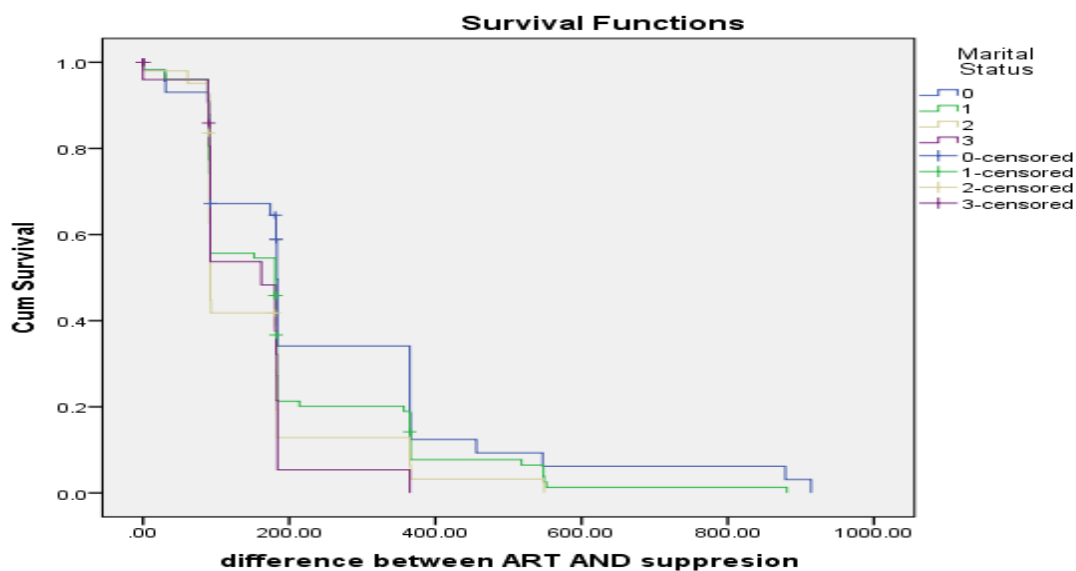


Figure 4. Survival curve for marital status of study participants in East Shewa Zone, Oromiya , Ethiopia, 2018.

Time to plasma viral load suppression with respect to occupation of participant showed there was no difference (log rank test χ^2 value 2.26, p-value 0.332) between outdoor and indoor work area. Median time to have an event was 182 days (CI: 177.2-186.7) for outdoor and 181 days (CI: 55.1-128.8) for indoor.

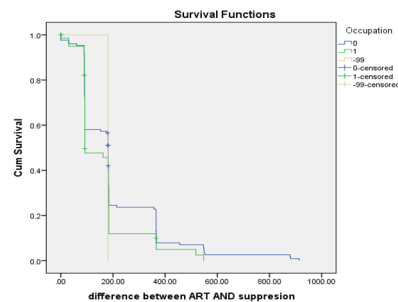


Figure 5. Survival curve between different categories of occupation for study participants in East Shewa Zone, Oromiya , Ethiopia, 2018.

Survival time in terms of viral suppression from HIV patient's plasma was not significantly different with respect to educational level. Log rank test for these variable was χ^2 value 3.40, p-value 0.334) and minimum median time was registered in illiterate patients with median time of 162 days (CI: 126.95-197.04) and maximum median time was observed in patients with higher education.

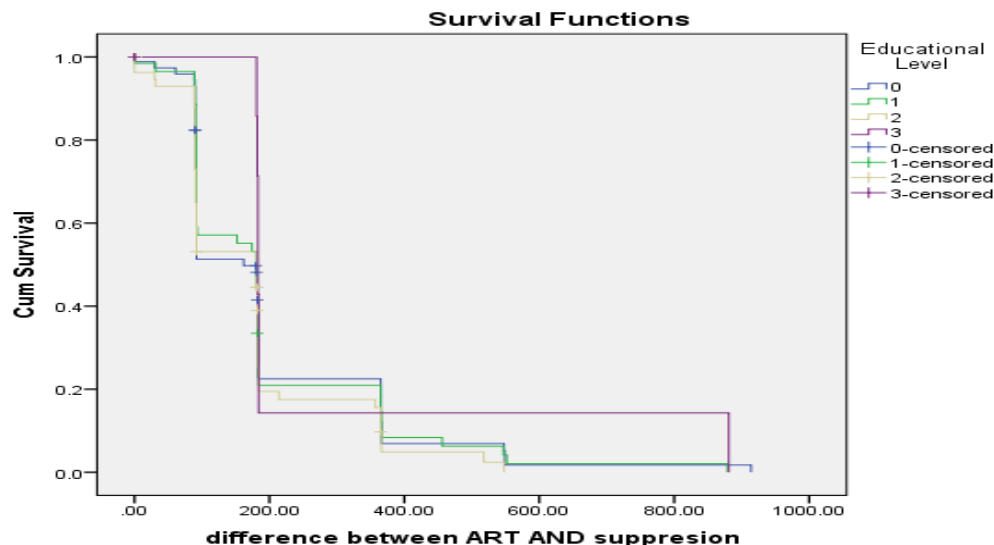


Figure 6. Survival curve between different educational levels of study participants in East Shewa Zone, Oromiya , Ethiopia, 2018.

Median time to viral load suppression in groups of HIV patients categorized based on their MUAC status showed no significant difference between the categories. Log rank test with χ^2 value 0.206, p-value 0.902). Maximum median time observed in MUAC category of >21 cm(181 days), while the minimum median time observed in MUAC category of < 18 cm with 92 days.

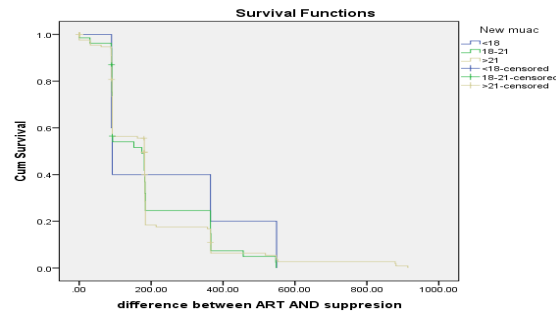


Figure 7. Survival curve between different educational levels of study participants in East Shewa Zone, Oromiya , Ethiopia, 2018.

In this study, similar survival curve was observed in BMI category. The log rank test with χ^2 value of 1.61 and p-value of 0.656 describes the similarity of the curves. BMI category of <18.5 kg/m² or underweight study participants estimated median time for suppression of 181 days (CI: 155.09-206.90), 18-24.9 kg/m² or normal BMI category with 181 days (CI: 155.35-206.64), BMI category of 25-29.9 kg/m² with median time of 90 days (CI: 0.00-186.00).

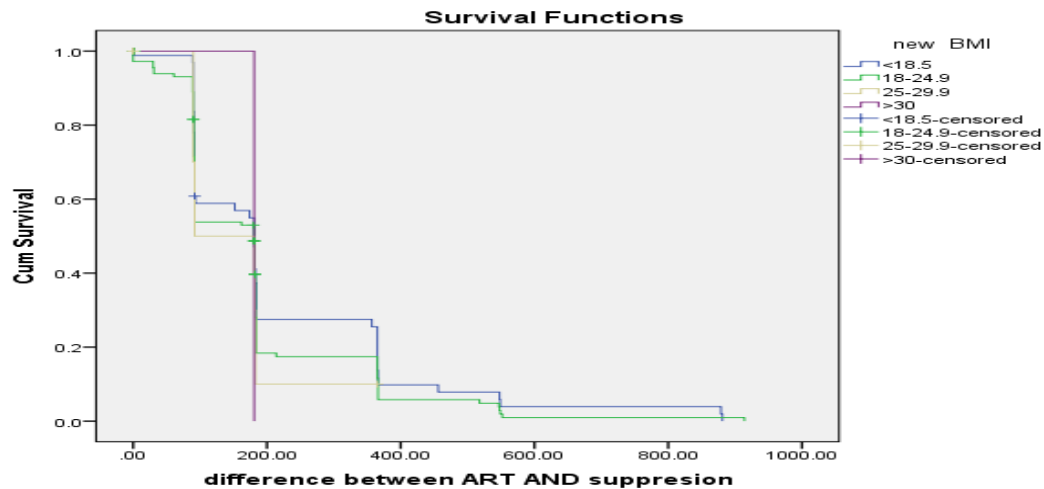


Figure 8. Survival curve between different categories of BMI of study participants in East Shewa Zone, Oromiya , Ethiopia, 2018.

Significant survival curve difference (log rank test: χ^2 value of 8.84 and p-value of 0.012) was observed in HIV patients with different baseline CD₄ count. Median survival time for patients with <200 cells/ μ l measured 182 days (CI: 160.80-203.19), 181 days (142.39-219.60) for BCD₄ 200-350 cells/ μ l, 174 days (CI: 133.40-214.59) and 174 days (CI: 133.40-214.59).

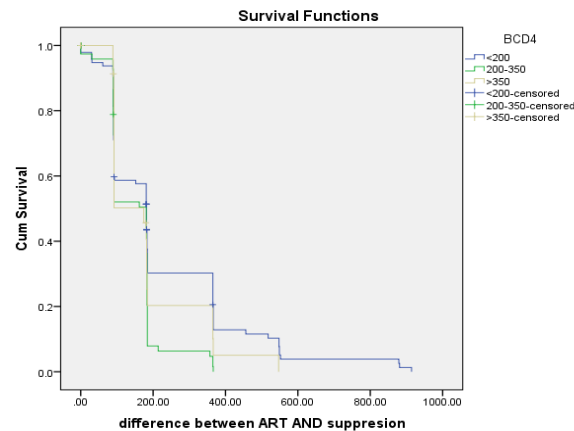


Figure 9. Survival curve between different categories of BMI of study participants in East Shewa Zone, Oromiya , Ethiopia, 2018.

Presence of Tuberculosis in HIV patients during enrollment of study participants showed no significant difference (log rank test: χ^2 value of 0.576 and p-value of 0.448). Median survival time for baseline TB positive patients were 92 days (CI: 91.42-92.57) compared with 182 days (CI: 177.70-186.29) for baseline TB negative patients.

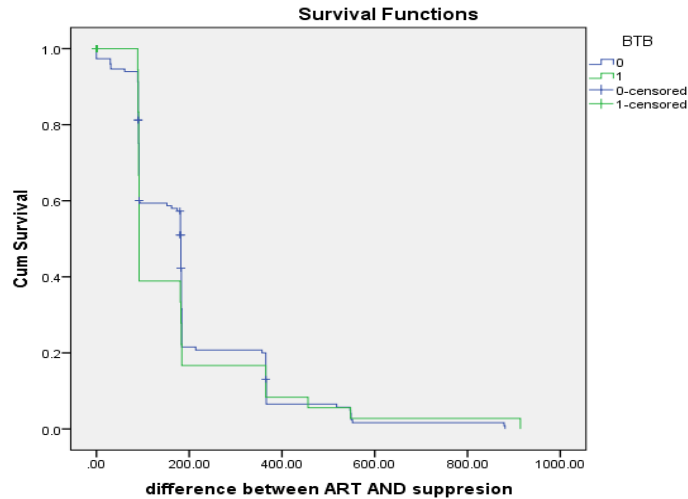


Figure 10. Survival curve between different categories of BMI of study participants in East Shewa Zone, Oromiya , Ethiopia, 2018

Multivariable analysis

IBM Inc. SPSS V. 21 software was used to determine factors affecting the median time to plasma viral load in the patient blood. Stepwise factor selection method was used to identify factors that are significantly affect the median time. Cox-proportional hazard regression method was used to estimate the magnitude of each variables. Variables with p-value of ≤ 0.05 were included in the model and selected as variables to fit a model that best explain the variance in the equation. Variables identified as significant in this study was marital status with p-value 0.023 and baseline CD₄ with p-value 0.023. Educational status (p-value 0.404), MUAC(p- value 0.407) BMI(p-value 0.335) and BTB(p-value 0.257).

The model fit and interpretation

$$h_i(t) = h_0(t) \exp(\beta_1 x_1 + \beta_2 x_2 + \beta_3 x_3 + \dots)$$

$$\log h(t) = \log h_0(t) + \beta_1 x_1 + \beta_2 x_2 + \beta_3 x_3 + \dots$$

$$\log h(t) = -1.16 \text{Marital status} - 0.556 \text{BCD}_4$$

The log hazard ratio of single marriage status study participant having viral load suppressed below detection level will be the same as baseline log hazard ratio. But the log hazard ratio for married patient to reach viral suppression level decrease by 1.16.

6. Discussion

Median time for plasma viral load suppression in the study cohort was determined using survival regression. Based on the study, median time for suppression was 181 days (CI: 140.5-221.4). This finding exactly matches with a study done by US department of health and human service in 2017, which found the median time between at about 24 weeks after initiation of ART. In another study conducted by Snippenburg W Van, Nellen FJB and Smith C, the median time to undetectable plasma viral load after initiation of treatment was found to be 60 days (12-168 days) which is lower than this study.

As of 2015, 72% of study participants achieved viral suppression, But in a study conducted in Brazil, the the percentage of HIV patients achieving viral suppression were 62%. This difference may be attributed due to the length of timing of follow up of the patients. Similar study conducted in neighboring Kenya revealed that only 39.85% of patients had virological suppression .In another study conducted by Shikuma CM and et al., the percentage of patients taking ART of different regimen reaching virological suppression after taking ART for 16 weeks showed 93% viral suppression. In this study, the percent of patients having virological failure was 16.5%. The same study by Shikuma CM and et al., found that 12.2% of patients have virological failure. Viral suppression rate of this study was found to be similar across different geographical spectrum. Study done in low and middle income countries of Brazil, Laos people's democratic republic, Malaysia, Mexico, Myanmar and republic of Moldova have achieved viral suppression of 80%.

Age category of 30-39 years old had minimum time to viral suppression with 92 days(CI: 60.1-123.8) and the maximum time to achieve viral suppression was found in age category of 50-59 years. Significant difference in proportion of different age group was not found by log rank test. In a study conducted in Kenya by Cherutich found significant difference between different age category in achieving viral suppression level. In this study there were significance difference between age group of 15-29 age group and 30-64 years category with the rate of 46.5% and 22.3% respectively.

significant sex difference was achieved in plasma viral load suppression among different sex category. Pearson's χ^2 for sex category was 5.06 with p-value of 0.024. Significant difference

between sex categories was also achieved in a study conducted by Ballesteros-zebad P. in Mexico, which found high suppression rate in male patients compared to Female patients. Other studied which found significant difference between male and female HIV patients viral suppression level was done by Pinto M. in southern Brazil, and Gray RH., in Uganda. Viral load suppression across sex category was not significant in a study done by Rangarajan S., Colby DJ in Vietnam. In this study, which is done in Vietnam, there was no significant difference between male and female HIV patients achieving undetectable viral level. In this study, Viral suppression among women was not significantly different with 93.7% vs 92.9% in male and female respectively.

The median baseline CD₄ was similar with study conducted in Northern Province, Cameroon with 204 cells/ μ l and 192 cells/ μ l respectively. Survival curve was not significantly different among different BCD₄ categories which is also a result supported by the above study mentioned, But similar study in Cameroon by Boelaert M. suggested significant difference in survival of patients between different BCD₄ category.

Baseline Mid upper arm circumference for evaluation of patients nutritional status does not appear to be associated with decrease in viral load suppression. Other studies suggested different association. A study by Liu E, Spiegelman D, found that base line lower MUAC was associated with lower rate of viral suppression from patient plasma.

Body Mass Index affected survival time of patient with χ^2 8.98 and p-value of 0.003. BMI category < 18.5 kg/m² had increased risk of higher viral replication in a study by Sharma A. and Hoover DR, but association between obesity and reduced or increased viral load was not observed.

No difference in survival curve of HIV patients to reach viral load level with respective to different ART treatment regimen. Snippenburg W. Van achieved the same curve property in a study, which found no difference between protease inhibitor and non-nucleoside reverse transcriptase inhibitor based regimens.

At least one instance of viral rebound was occurred in 16.5% of cohort of HIV patients in the study period. This figure was 45.1% in the study performed by Guillemi S, Hogg R, Montaner J.

equals to crude incidence of viral rebound of 12.6% compared to 16.4% crude incidence of viral rebound in this study.

Variables identified as significant in this study was marital status (p-value 0.023) and baseline CD4 (p-value 0.023). Pinto et al, found significant effect of age and ART usage on survival of patient taking ART drugs. Body mass index, sex , WHO clinical stage and hemoglobin level were cited as significant independent predictors of plasma viral load level in the patient plasma.

Educational status (p-value 0.404), MUAC(p- value 0.407) BMI(p-value 0.335) and BTB(p-value 0.257). There were no significant association found in the percentage of patients with undetectable viremia by sex, marital status, educational level residence or wealth index(Rangarajan S, Colby DJ). Gray RH and et al, found significantly higher viral load after ART treatment in male and concurrent infection with Tuberculosis, Herpes virus, malaria and helmentiasis. Study done by Semu H. and Hawkin C. also confirm that baseline MUAC and plasma viral load level does not have significant relation.

7. Limitation of the study

Sample size was not adequate to detect minimum survival difference in different study category. to study time to PVL suppression, the study needs BPVL. The number of patients with BPVL was only 243.

8. Conclusion

Viral rebound was seen in 16.5% of study participant. The Proportion of patients having PVL suppressed after taking ART was 72.4%. The maximum median time for PVL suppression was observed in unmarried participants with 183 days. The minimum median time registered in divorced participant category with estimated median time of 92 days. The maximum median time for PVL suppression was observed in unmarried participants with 183 days. The minimum median time registered in divorced participant category with estimated median time of 92 days.

Estimated time to achieve PVL after taking ART was found to be 181 days. Factors affecting time to suppression level was marital status and baseline CD4. Additional factors believed to be influencing survival curve were also studied, but not significant relation was found with the response variable.

9. Recommendation

Ministry of health should focus on improving nutritional status of HIV patients taking ART.

Further study should be conducted by increasing the sample size and study area for better interpretability of the investigation.

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Declaration

I, the undersigned declare that this thesis is my original work in partial fulfillment of the requirement for the degree of Master of Public Health. I also declare that it has never been presented in this or any other university and that all resources and materials used in the thesis have been duly acknowledged.

Student Name: _____

Signature: _____

Place of submission: _____

Date of submission: _____

This thesis has been submitted with my approval as a College/university advisor.

Primary Advisor Name: _____

Signature: _____

Date of submission: _____

Secondary Advisor Name: _____

Signature: _____

Date of submission: _____