# Serum lipid profiles of patients taking efavirenz based antiretroviral regimen compared to ritonavir-boosted atazanavir with an optimized back ground at Zewditu Memorial Hospital, Addis Ababa, Ethiopia

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**Research**

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# Abstract

**Background:** Dyslipidemia represent significant health care concerns in Human immune deficiency virus (HIV) infected patients taking highly active antiretroviral therapy due to their association with cardiovascular disease risk. There is limited data regarding the effects of boosted atazanavir (ATV/r) treatment in the lipid profiles of Ethiopian HIV patients. Thus, this study compares the lipid profile changes of HIV patients on ATV/r-based regimen compared to efavirenz (EFV)-based regimen, while the background nucleos/tide backbone is optimized.

**Materials and methods:** A comparative Hospital based cross-sectional study was conducted among adult HIV-infected patients at Zewditu Memorial Hospital, Addis Ababa, Ethiopia, from July-September 2017. Equal number of EFV and ATV/r-treated patients (n = 90 each) taking for one year and above were included in the study. Serum lipid parameters (triglyceride (TG), total cholesterol (TC), high density lipoprotein cholesterol (HDL-C), and low density lipoprotein cholesterol (LDL-C)) were measured using fully automated mind ray, Chemistry analyzer. Data comparison used chi-square test, Student t-test and Mann-Whitney U test. Multivariate regression analysis and p-value<0.05 was used to identify associated factors of serum lipid profiles.

**Results:** In the present study ATV/r-treated group resulted significantly higher in the median values of TG [207 (56-1094) vs. 145(42-768) mg/dL; p=0.001] and the mean value of TG/HDL-C ratio (6.6 vs. 4.4; p=0.001) as compared to EFV-treated group. EFV-treated group showed significantly higher in the mean value of HDL-C (44.7 vs. 38.7mg/dL; p= 0.001) as compared to ATV/r-treated group. No significant difference was found in TC (p=0.5), LDL-C (p=0.6), TC/HDL-C (p=0.5) and LDL-C/HDL-C (p=0.1) between EFV and ATV/r-treated patients. In ATV/r-treated patients, CD4 count and body mass index (BMI) was significantly associated with TC. In EFV-treated patients, BMI was significantly associated with increased serum LDL-C and TC in female participants.

**Conclusion:** In conclusion, ATV/r raises TG and TG/HDL-C while, HDL-C was higher in EFV than ATV/r-treated group. Both groups have less atherogenic lipid profiles in terms of TC/HDL-C and LDL/HDL-C.


# Introduction

HIV patients taking antiretroviral drugs have been associated with a number of metabolic and anthropometric abnormalities including dyslipidemia, lypodystrophy and insulin resistance [1], all of which may contribute to an increased risk of cardiovascular disease (CVD) [2]. From the class of ART drugs, protease inhibitors are the most widely implicated drug class in early on-set CVD, but non-nucleoside reverse transcriptase (NNRTI's) have also been implicated.

Efavirenz (EFV) and ritonavir-boosted atazanavir (ATV/r) are two commonly used antiretroviral drug [3]. Compared to other protease inhibitors, atazanavir has no adverse impact on cholesterol, triglyceride, and other metabolic parameters, including insulin and glucose [4]. In addition, in patients who developed hyperlipidemia due to prior Highly Active Anti-Retroviral Therapy (HAART) regimens, atazanavir has been

shown to decrease lipid concentrations to near normal levels [5, 6]. EFV is a beneficial effect in the protective high density lipoprotein-cholesterol (HDL-C) and related to EFV plasma concentrations [7].

A pressing need remains to better quantify non-AIDS related co-morbidities in people living with HIV in Sub-Saharan Africa. Most studies of cardiovascular co-morbidities with HIV represent populations from developed countries. The treatment disparities, however, between the developing world and the developed world remain great. For instance, EFV and ATV/r based regimen is first-line treatment in developed world while in Ethiopia ATV/r based regimen is second-line treatment regimen. These treatment disparities, combined with differences in demographics, lifestyle, and nutritional status between Ethiopian and Western populations, may make this population more susceptible to non-AIDS related co-morbidities.

WHO recommends that EFV as part of first-line therapy and ATV/r as part of second-line therapy. In resource-limited settings, EFV and ATV/r remain cornerstones of ART. The comparative safety of regimens based on ATV/r and EFV are, however, incomplete. Most studies come from the developed world. Very limited comparative data exist for ATV/r and EFV, both used in combination with Tenofovir Disoproxil Fumarate (TDF) and Lamivudine (3TC) on serum lipid profiles.

Therefore, the present study will compare serum lipid profiles between EFV and ATV/r-treated adult HIV patients and assess associated factors of serum lipid profiles in the study area and give recommendations so as to minimize CVD morbidities and mortalities. We hypothesized there is difference in mean values of serum lipid profiles of adult HIV-1 infected patients taking between EFV and boosted ATV based regimens.

# Materials And Methods

The study was conducted at ART Clinic of Zewditu Memorial Hospital (ZMH), Addis Ababa, Ethiopia from July 1/2017–June/2018. Hospital based cross-sectional study design of comparative nature was conducted.  90 EFV and 90 ATV/r containing regimens participates in this study.

Age greater than or equal to 18-year-old HIV-positive patients on EFV- and ATV/r-containing regimens for at least one year were recruited to participate in this study. Subjects were excluded if they had active AIDS defining illnesses, thyroid disorders or diabetes mellitus. Subjects fasted and refrained from tobacco products for at least 8 hours prior to the test.

Participant age, sex, HIV-sero status, date of first HIV-sero positive test, initial CD4+ cell count, last CD4+ cell count, and any viral load determinations, and date of initiation of current and all previous HAART regimens were obtained from the participants hospital card. Questionnaire-driven interviews were performed by a trained research nurse at the ZMH HIV clinic. Self-reported personal and familial (mother, father, brothers, or sisters) history of heart attack, kidney disease, diabetes, or lipid disorders and self-reported alcohol and cigarette use were recorded.

### Anthropometric measurements

The weight of the study participants was measured using a standard balance, and the height was measured by using a height-measuring device attached to the balance. Body mass index (BMI) was calculated by dividing weight (kg) by height ($m^2$). Using the WHO classification, four categories of BMI can be identified as follows: underweight, <18.5 kg/$m^2$; normal, >18.5–24.9 kg/$m^2$; overweight, >25.0–29.9 kg/$m^2$; and obesity, >30 kg/$m^2$ [8].

Waist and hip circumference of the patients were also measured. Waist circumference was measured over light clothing at the level halfway between the iliac crest and the costal margin in the mid-axillary line after exhaling, when the lungs were at their functional residual capacity, with the subject in standing position with the body weight evenly distributed across the feet. Hip circumference was measured over light clothing at the level of greater trochanters with the subject in standing position and both feet together.

While the cut-off point considered for waist circumference (WC) was >80cm for females and >90cm for males to define overweight, the cut-off taken for waist to hip ratio was >0.8 for females and >0.9 for males as per the criterion of the WHO [9].

### Blood sample collection and analysis

For determination of serum lipid profiles such as TC, TG, HDL-C and LDL-C, after overnight fasting, 5 ml venous blood sample was collected from both groups by phlebotomy laboratory technician under aseptic conditions. Measurement of serum samples such as serum TC, TG, LDL-C and HDL-C were assessed using calibrated fully automated Mind ray BS-200E, clinical chemistry analyzer (China) according to the reagent manufacturer's instruction in central laboratory of ZMH.

### Data processing and analysis

Data was checked, cleaned and entered in to Epi-data software version 3.1, and then it was exported to SPSS version 22.0 software for analysis. The results of the descriptive statistics were expressed as frequency and percentage. Chi-square ($\chi 2$) test was used to compare categorical variables. Continuous variables were presented as mean ± standard deviation and median (Inter quartile range). Student t-test was performed to detect differences between groups on continuous variables that did show normality. While Mann-Whitney U test was performed on continuous variables that did not show normality.

Correlation analysis was performed and multivariable linear regression models were constructed to examine the association of independent variables with TC, LDL-C and HDL-C for all study participants. Relevant independent variables were selected for the inclusion of the initial models and the stepwise fit multivariable regression, which eliminates (or adds) covariates in a stepwise fashion, was used with the criteria $p<0.05$ for removal from (or inclusion in) the final model.

## Results

## General characteristics of study participants

One hundred eighty (90 EFV and 90 ATV/r) treated adult HIV-1 infected patients participated in this study. The mean age for EFV and ATV/r treated patients was 41.2 ± 8.8 and 42.2± 8.8 years old respectively. Therefore, EFV and ATV/r treated adult HIV-1 infected patients were age-matched (Independent Samples T-test, % CI = 95, p-value = 0.4). The number of females were 55/90 (61.1%) in the EFV-treated group and 52/90 (57.8%) in the ATV/r-treated group. So, the sex of EFV-treated patients was well matched with the ATV/r-treated patients (chi-square test, % CI=95, p-value = 0.7) (Table 1).

The clinical features obtained from patients' medical records showed that, the median last $CD4^+$ cell count was lower in ATV/r-treated as compared to EFV-treated group. Months since first HIV positive diagnosis were higher in ATV/r-treated group as compared to EFV-treated group. ATV/r-treated group was on HAART longer than EFV-treated group. Patients in EFV-treated group have been on their current regimen longer than ATV/r-treated group (Table 1). Considering history of hypertension and family history of lipid disorder, all of the study participants responded 'no'. Considering smoking status, all of 180 participants responded 'no' for current smoking status. Self-reported treatment or drug adherence rate showed that ≥ 95% or good drug adherence in both groups. In the present study, no differences were observed in the average BMI of the two groups.

## Serum lipid levels of study participants

Lipid profile tests (TC, TG, HDL-C and LDL-C) were performed for 180 (90 EFV& 90 ATV/r)-treated participants. According to the results, TG ≥200mg/dL was detected in 24/90 (26.7%) of EFV-treated group and 47/90 (52.2%) of ATV/r-treated group. HDL-C<40mg/dL was detected in 35/90 (38.9%) of EFV-treated group and 47/90(52.2%) of ATV/r-treated group. The ratio of TC/HDL-C ≥5 was detected in 24/90 (26.7%) of EFV-treated group and 29/90 (32.2%) of ATV/r-treated group (Table 2).

The results of this study also showed that the median serum TG level of EFV and ATV/r-treated based participants was 145 (42- 768) mg/dL and 207 (56-1094) mg/dL. The average level of serum HDL-C was found to be 44.7 ±12.4mg/dL and 38.7±9mg/dL in EFV and ATV/r-treated groups respectively (figure 1).

Independent sample t-test was performed to see if there was statistical significant difference in the mean values of serum TC, LDL-C and HDL-C between EFV and ATV/r-treated adult HIV-infected patients. It was found that the mean level of serum HDL-C was significantly lower in the ATV/r-treated group than EFV-treated group (p=0.001) (Fig. 1).

Mann-Whitney U test was performed to see if there was statistical significant difference in the median serum TG value. It was found that the median value of serum TG was significantly higher in the ATV/r-treated group than EFV-treated group (p=0.001) (Fig. 1).

The average TG/HDL-C ratio was 4.4±3.6 in EFV-treated group and 6.6± 5.5 in ATV/r-treated group. The mean LDL-C/HDL-C ratio was 3.1±1.2 in EFV-treated group and 3.4±1.2 in ATV/r-treated group (Fig.2).

Independent sample t-test was done to see if statistical significant difference in the mean ratios of TC/HDL-C, TG/HDL-C and LDL-C/HDL-C. It was found that mean TG/HDL-C ratio was significantly higher in ATV/r-treated group than EFV-treated group (p=0.001) (Fig. 2).

Considering sex, in female EFV- and ATV/r-treated adult HIV-1 infected patients, the median values of TG were 123(42-768)mg/dL and 184(71-481)mg/dL; the average values of HDL-C were found to be(46.3±13.3 and 39.8 ±8.7 mg/dL) respectively. In addition, the results of the present study showed that in the serum of male EFV and ATV/r-treated HIV-1 infected patients, the mean values of LDL-C were 140.4±48.9mg/dLand118.9±40.8 mg/dL(Table 3).

### Correlation and regression analysis of lipid profiles with predictors in ATV/r-treated group

Bivariate, Pearson correlation test was carried out to determine any association (relationship) between serum levels of lipid profiles and clinical characteristics. Last CD4 count was positively correlated and significant with TC (r=0.286, p=0.02) and HDL-C (r=0.206, p=0.02). Serum LDL-C level was significantly associated with sex (p=0.02). Waist circumference and waist-hip ratio was correlated with TC among female participants (p=0.008 and p=0.04) respectively (Table 4). Multivariate regression analysis was done for predictors to the dependent variables and found TC level was associated with CD4 count (adjusted $R^2$ =0.082, β-coefficient=0.06, p=0.006). Again TC level was associated with waist circumference among female participants (adjusted $R^2$= 0.146, β-coefficient=0.409, p=0.008) (Table 4).

### Correlation and regression analysis of lipid levels with predictors in EFV-treated group

The analyses showed that serum LDL-C level was significantly correlated with duration of HIV positive since first diagnosis (p=0.04). It also correlated with waist hip ratio (p=0.02) and BMI (p=0.001) among female participants. Serum TC levels was significantly correlated with waist circumference (p=0.02) and BMI (p=0.001) among female participants (Table 5). Multivariate regression analysis was done for all predictors to the dependant variables and found that BMI was associated with LDL-C levels (Adjusted $R^2$ =0.170, β-coefficient=0.430, p=0.01) and TC levels (adjusted $R^2$=0.209, β coefficient= 0.473, p=0.001) in female participants (Table 5).

# Discussion

With rapid scale up of ART and the increasing usage of antiretroviral drugs to prevent HIV, the need to monitor side effects of these drugs has increased substantially. HIV-infected patients are known to have an increased risk of CVD compared with the general population, with a significantly elevated mortality rate from cardiovascular events [10]. Dyslipidemia represents significant health care concerns in HIV infected patients due to its direct association with increased CVD risk [11]. So that assessing of serum lipid profiles in HIV patients on ART help in early prediction of CVD.

The results of the current study revealed that there was a statistically significant difference between ATV/r- and EFV-treated groups in median TG values (p=0.011) (Figure 1). The likely explanation of

elevated levels of TG on the ATZ/r-treated group might be due to the addition of low dose ritonavir which increases significantly serum or plasma TG levels [12, 13]. The results of our study are similar to those observed in comparative trails comparing EFV and ATV/r [14].

The study participants having TG ≥200mg/dL were higher in ATV/r-treated group (52.2%) as compared to EFV-treated group (26.7%). For ATV/r-treated group, it was higher than the prevalence reported from the study conducted in Barcelona-Spain by Podzamczer et al. [15] that compared ATV/r to nevirapine and found that 37.8% abnormal TG levels. This variation might be due to difference in the socio-economic status of study participants and duration of exposure to the treatment. The other possible explanation might be that some of the study participants in Podzamczer et al.'s study were on lipid lowering drugs.

For EFV-treated group, it was lower than the prevalence reported from the study conducted in Addis Ababa-Ethiopia by Belay et al. [16] which was 36.6%. This variation might be due to difference in the cut-off value used and sample size. In Belay et al., the cut of value was TG ≥ 150 mg/dL, which is lower than that used in our study (TG≥200mg/dL). Another possible explanation might be treatment duration that may contribute to the difference.

The average value of HDL-C was significantly lower (p=0.001) in the ATV/r-treated group as compared to EFV-treated group (Figure 1). Similar results were found in a randomized control trails that reported lower HDL-C in ATV/r-treated group than in EFV-treated group [17, 18]. Several confounding factors contribute to our observation. First, duration of current treatment with EFV-treated group is nearly double that of the ATV/r-treated group. Second, CD4 count was higher in the EFV-treated group as compared to ATV/r-treated group.

Available data also suggested that a long term therapy with EFV and its concentration is directly proportional to HDL-C levels [7]. In addition, genetic variation may also be attributed to the changes in HDL-C levels [19]. Interestingly, it has been shown that efavirenz-induced increase in HDL-C is influenced by the gene multi drug reasistance-1(MDR-1) polymorphism that codes for the drug transporter P-glycoprotein. Differences in the *MDR-1* gene polymorphism have been related to the EFV concentration in plasma and to the immune recovery of CD4 lymphocyte cell counts [20].

The possible molecular mechanism by which EFV increase the HDL-C levels were through down regulation of the activity of the plasma cholesterol transfer protein (CETP) expression through antagonism of the lipid transcription factor, LXR. CETP, which is known to regulate human lipoprotein cholesterol ester to TG exchange and affect HDL-C levels [21].

In the same pattern, the average ratio of TG/HDL-C was significantly higher (p=0.001) in the ATV/r-treated group as compared to EFV-treated group of the present study (Figure 2). This is due to high levels of TG and low levels of HDL-C on the ATV/r-treated group as a result their ratio became high. Even if there is no similar study regarding the TG/HDL-C ratio, it has greater predictive power than each of the single standard lipid parameters and superior to the other ratios in order to predict insulin resistance [22]. Furthermore, a TG/HDL-C ratio of ≥3 has been shown to be closely correlated to insulin resistance [23].

However, the capacity of TG/HDL-C to predict insulin resistance may vary by race. For example, a study done in South Africa among overweight women that includes West Africa, Black South Africans and African Americans showed that the TG/HDL-C ratio was not predict insulin resistance [24]. On the other hand, studies in overweight women of Whites suggest that the TG/HDL-C ratio effectively identifies insulin resistance. Yet, the pattern of the dyslipidemia of insulin resistance differs in African Americans and Whites, and therefore the ability of the TG/HDL-C to predict insulin resistance may vary by race. In Whites, the dyslipidemia of insulin resistance follows the classic pattern of elevated TG and low HDL-C. However, in African Americans, West Africans and Black South Africans, normal TG with low HDL-C is the characteristic lipid profile of insulin resistance [25].

The mean values of TC and LDL-C were not show statistically significant differences between EFV and ATV/r-treated groups. However, the mean values of TC and LDL-C were slightly higher in EFV-treated group as compared to ATV/r-treated group. This is corroborated by the results of Ganesan et al. [18] and Squires et al. [17]. The higher TC in EFV-treated participants is likely due to both higher HDL-C and LDL-C values.

Similarly, it was found that both groups were not significantly different in the mean ratios of TC/HDL-C and LDL-C/HDL-C. In comparison to EFV, ATV/r-treated group was slightly higher in mean values of TC/HDL-C and LDL-C/HDL-C. Michael and Heneri [14] and Gotti et al. [26] also reported that both EFV and ATV/r-treated adult HIV patients were similar in mean ratios of TC/HDL-C. TC/HDL-C and LDL-C/HDL-C ratios are indicator of CVD risk with greater predictive value than isolated parameters used independently [27]. The predictive capacities of these ratios are supported by data suggesting that an increase in HDL-C is more prevalently associated with plaque regression. This may be particularly interesting in patients with features of the metabolic syndrome [28].

The current study had investigated the associations of some demographic, clinical features and anthropometric indices (BMI, WC, and waist-to-hip ratio) and lipid abnormalities in EFV- and ATV/r-treated group. Accordingly, CD4 count showed significantly positive association with serum TC levels among study participants on ATV/r-treated group. In agreement with the results of this study, Belay et al. [16] and Kamoru et al. [29] reported significantly positive correlation with CD4 among HAART patients. Waist circumference also significantly associated with TC among female participants in ATV/r-treated group. In agreement with these results, a study done by Beraldo et al. [30] reported significant association between waist circumference and TC levels.

An increased waist circumference is most likely associated with elevated risk factors of CVD because of its relation with visceral fat accumulation, and the mechanism may involve excess exposure of the liver to fatty acids and release of detrimental adipocytokines and lower levels of beneficial adipocytokines and these have multiple detrimental effects, including proinflammatory damage, altered signaling pathways and reactive oxygen species production, on beta cells and other tissues resulting in disease states like hypertension and diabetes [31].

Increased BMI showed significantly positive association with serum TC and LDL-C among female participants in the EFV-treated group. Importantly, anthropometric indicators in male participants were not significant determinants of any lipid variables in both groups. The reason behind this was unclear.

There was no statistically significant association observed between HDL-C and TG levels with predictor variables. Similar finding had been reported in studies conducted in London [32]. There was no association between duration of HIV positive since first diagnosis and duration on HAART and serum lipid parameters in both groups. These results agree with the study results of Nery et al. [33]. The observed difference between EFV and ATV/r-treated groups on associated factors of serum lipid levels was unknown.

Our study needs to be interpreted in the light of its limitations. The cross-sectional design precludes causal associations between dyslipidemia and patient characteristics. The study did not include a control group of HIV-uninfected persons which would have provided better insight into the role of HIV infection and antiretroviral drugs. There were baseline differences of the two groups on CD4 count, duration with HIV, duration on HAART and duration on current treatment so it may be affect the outcome variables.

# Conclusion

The results of the present study evaluated serum lipid profiles of ATV/r compared with EFV-treated groups, when combined with TDF/3TC. Our research found that ATV/r raises TG and TG/HDL-C while, HDL-C was higher in EFV than ATV/r-treated participants. Even though there were no statistically significant differences, the mean values of TC and LDL-C were slightly higher in EFV- than in ATV/r-treated group. The ratio of TC/HDL-C and LDL-C/HDL-C was higher in ATV/r- than EFV-treated group. Therefore, we accept the alternative hypothesis stating that there is a difference in lipid profiles between EFV and ATV/r-treated groups. Assigning conventional risk increments to lipoprotein fraction changes, EFV-treated patients would on balance likely have lower cardiovascular risk due to their substantially increased HDL-C in the face of a modest increase in TC resulting in a lower TC: HDL-C ratio.

This study also showed that CD4 count showed statistically significant association with TC levels among ATV/r-treated group. Waist circumference also associated with TC in female participants of ATV/r-treated group. TC and LDL-C were associated with BMI among female participants in EFV-treated group.

# Abbreviations

3TC Lamivudine

AIDS Acquired Immune Deficiency Syndrome

ART Anti Retroviral Therapy

ATV Atazanavir

ATV/r Ritonavir-boosted atazanavir

BMI Body Mass Index

CD4 Cluster of Differentiation four

CVD Cardio Vascular Disease

EFV Efavirenz

HAART Highly Active Anti Retroviral Therapy

HDL-C High Density Lipoprotein- Cholesterol

HIV Human Immune Deficiency Virus

LDL-C Low Density Lipoprotein-Cholesterol

NNRTI Non Nucleoside Reverse Transcriptase Inhibitor

NRTI Nucleoside Reverse Transcriptase Inhibitor

NtRTI Nucleotide Reverse Transcriptase Inhibitor

NVP Nevirapine

SPSS Statistical Package for Social Sciences

TDF Tenofovir Disoproxil Fumarate

TG Triglyceride

TC Total Cholesterol

TC/HDL-C Total Cholesterol/High Density Lipoprotein-Cholesterol

TG/HDL-C Triglyceride/High Density Lipoprotein-Cholesterol

WHO World Health Organization

ZMH Zewditu Memorial Hospital

# Declarations

### Ethical approval and consent to participate

Ethical approval was obtained from the Departmental Research and Ethics Review Committee, Department of Biochemistry, College of Health Sciences, Addis Ababa University. Collaboration letter for data collection was also obtained from ZMH.

Collaboration letter for data collection was also obtained from ZMH. The objective of the study was briefly clarified and explained for each participant, before enrolling any of the eligible study participants. Samples and data were collected after informed consent had been obtained from the study participants. To assure confidentiality, a code number was used instead of the participants' name or identification number.

### Consent for publication

Not applicable

### Availability of data and materials

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

### Competing interest

The authors declare that they have no competing interest.


### Funding

The funders had no role in the design of study, data collection and analysis, and interpretation of data and in writing the manuscript.


### Authors' contributions

All authors contributed to the design of the study and the interpretation of data. However, Abebe Muche performed the data analysis and compiled the whole work as well as drafting the paper Menakath Menon edited the language and critically commented on the paper. All the authors critically revised, read, and approved the final paper.


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# Tables

**Table 1: Baseline characteristics of study participants**

| Variables | EFV-treated n=90 | ATV/r-treated n=90 | p-value |
|---|---|---|---|
| Age, [mean (SD)] | 41.2±8.8 | 42.2±8.8 | 0.4 |
| Sex, Female [n (%)] | 55 (61.1%) | 52 (57.8%) | 0.7 |
| CD4+ count at enrolment(cell/ml) [median (IQR)] | 454 (103-1655) | 355 (40-1041) | **0.002*** |
| Viral load determined last 6 months [n (%)] | 39 (43.3%) | 40 (44.4%) | 0.7 |
| Undetectable viral load (<50copies/cell) [n (%)] | 35 (89.7%) | 30 (75%) | 0.2 |
| Months since first HIV diagnosis [median (IQR)] | 108 (16-164) | 138 (35-240) | **<0.001*** |
| Months on HAART [median (IQR)] | 89 (15-163) | 133 (34-174) | **<0.001*** |
| Months on current regimen [median (IQR)] | 48 (15-156) | 25 (13-44) | **<0.001*** |
| Prophylaxis drugs for OIs [n (%)] | 12 (13.3) | 12 (13.3) | 1.0 |
| Body mass index [mean SD] | 25.0±4.2 | 24.3±4.4 | 0.2 |
| <18 [n (%)] | 4 (4.4%) | 5 (5.6%) | 0.6 |
| 18-24 [n (%)] | 41 (45.6%) | 48 (53.3%) | |
| 25-30 [n (%)] | 35 (38.9%) | 30 (33.3%) | |
| >30 [n (%)] | 10 (11.1%) | 7 (7.8%) | |
| Waist circumference | | | |
| Male >cut off value [n (%)] | 14 (40%) | 15 (30.6%) | 0.5 |
| Female >cut off value [n (%)] | 34 (61.8%) | 24 (58.5%) | 0.9 |
| Waist to hip ratio | | | |
| Male >cut off value [n (%)] | 10 (28.6%) | 5 (10.2%) | 0.06 |
| Female >cut off value [n (%)] | 17 (30.9%) | 8 (19.5%) | 0.06 |
| Physical exercise [n (%)] | 54 (60%) | 50 (55.6%) | 0.7 |

| | | | |
|---|---|---|---|
| Alcohol drinking habit [n (%)] | 10 (11.1%) | 4 (4.4%) | 0.6 |

Key: Continuous variables are reported as mean (SD) and median (IQR), categorical variables are reported as number and percentage, SD= Standard Deviation, IQR= Inter Quartile Range,*= statistically significant by using chi-square tests (categorical) or Mann Whitney U test and Independent t-test (continuous), EFV= Efavirenz, ATV/r=Ritonavir-boosted atazanavir. OIs= Opportunistic Infections, n= number, %= percentage

**Table 2: Abnormal levels of lipid profiles in EFV and ATV/r- based regimen**

| Variables | Categories | EFV-treated (n=90, %) | ATV/r-treated (n =90, %) | p-value |
|---|---|---|---|---|
| Total dyslipidemia | Present n (%) | 73 (81.1) | 77 (85.6 ) | 0.5 |
| TC | ≥200 mg/dL | 25 (27.8) | 26 (28.9) | 0.9 |
| TG | ≥200 mg/dL | 24 (26.7) | 47 (52.2) | **0.01*** |
| LDL-C | ≥129 mg/dL | 49 (54.4) | 41 (45.6) | 0.3 |
| HDL-C | <40 mg/dL | 35 (38.9) | 47 (52.2) | 0.1 |
| TC/HDL-C ratio | ≥5 | 24 (26.7) | 29 (32.2) | 0.5 |

Key: n= number, %=percentage TC = Total Cholesterol, HDL-C = High-Density Lipoprotein-Cholesterol, LDL-C = Low Density Lipoprotein-Cholesterol, TG = triglyceride, TC/HDL-C ratio = Total cholesterol/High-Density Lipoprotein-Cholesterol ratio, EFV= Efavirenz, ATV/r= Ritonavir-boosted atazanavir, *= statistically significant.

**Table 3: Lipid levels of study participants of EFV and ATV/r-treated male and female adult HIV patients**

| Lipid panels in (mg/dL) | Female | | | Male | | |
|---|---|---|---|---|---|---|
| | EFV | ATV/r | p-value | EFV | ATV/r | p-value |
| TC(mean, SD) | 176.4±32.8 | 189.7±54.5 | 0.1 | 196.1±50.4 | 171.1±44.1 | **0.02*** |
| TG(median(IQR)) | 123(42-768) | 184(71-481) | **0.001*** | 210(71-768) | 219(56-1094) | 0.9 |
| LDL(mean, SD) | 125.4±38.8 | 138.1±46.8 | 0.1 | 140.4±48.9 | 118.9±40.9 | **0.03*** |
| HDL(mean, SD) | 46.3±13.3 | 39.8±8.7 | **0.01*** | 42.4±10.6 | 37.8±9.3 | **0.04*** |

Key: EFV=Efavirenz, AVR/r= Ritonavir boosted atazanavir, SD= Standard deviation, *statistically significant difference, TC= Total Cholesterol, TG= Triglyceride, LDL-C= Low Density Lipoprotein-Cholesterol, HDL-C= High Density Lipoprotein Cholesterol.

**Table 4: Correlation analysis of lipid profiles with predictor variables in ATV/r-treated group (N=90)**

| Predictors | TC | | LDL-C | | HDL-C | | TG | |
|---|---|---|---|---|---|---|---|---|
| | r | p | r | p | r | p | ρ | *p* |
| Age | -0.036 | 0.8 | -0.046 | 0.9 | -0.060 | 0.8 | 0.044 | 0.7 |
| Sex | -0.187 | 0.06 | -0.215 | 0.02 | -0.110 | 0.2 | 0.180 | 0.08 |
| Physical exercise | -0.023 | 0.5 | -0.058 | 0.8 | 0.087 | 0.3 | -0.085 | 0.4 |
| Cd4 count | 0.286 | **0.02** | 0.196 | 0.3 | 0.206 | 0.02 | 0.042 | 0.7 |
| HIV + since 1st diagnosis | 0.091 | 0.7 | 0.176 | 0.9 | -0.069 | 0.7 | 0.133 | 0.2 |
| Duration on HAART | 0.104 | 0.6 | 0.166 | 0.6 | -0.080 | 0.6 | 0.135 | 0.2 |
| Duration on ATV/r | 0.080 | 0.4 | 0.171 | 0.09 | 0.123 | 0.2 | 0.058 | 0.6 |
| Female anthropometric indicators | | | | | | | | |
| Waist circumference | 0.409 | **0.008** | 0.275 | 0.08 | 0.205 | 0.2 | -0.133 | 0.5 |
| Waist to hip ratio | 0.318 | **0.04** | 0.121 | 0.4 | 0.134 | 0.4 | -0.088 | 0.6 |
| Body mass index | 0.264 | 0.1 | 0.137 | 0.4 | 0.162 | 0.3 | 0.160 | 0.3 |
| Male anthropometric indicators | | | | | | | | |
| Waist circumference | 0.237 | 0.1 | 0.264 | 0.06 | 0.196 | 0.2 | 0.151 | 0.6 |
| Waist to hip ratio | 0.211 | 0.1 | 0.259 | 0.07 | 0.098 | 0.5 | 0.112 | 0.7 |
| Body mass index | 0.238 | 0.1 | 0.234 | 0.1 | -0.160 | 0.3 | 0.00 2 | 0.5 |

Key: r= Pearson correlation coefficient, p= p value for Pearson correlation, ρ = Spearman Rank Correlation Coefficient, P = p-value for Spearman correlation, TC =Total Cholesterol, TG= Triglyceride, LDL-C= Low Density Lipoprotein-Cholesterol, HDL-C= High Density Lipoprotein-Cholesterol, HIV= Human Immune Deficiency Syndrome Virus, HAART= Highly Active Anti Retroviral Therapy, CD4= Cluster of Differentiation, ATV/r= Ritonavir-boosted atazanavir.

**Table 5: Correlation analysis of lipid profiles with predictor variables in EFV-treated group (N=90)**

| Predictors | TC | | LDL-C | | HDL-C | | TG | |
|---|---|---|---|---|---|---|---|---|
| | r | p | r | p | r | p | ρ | *p* |
| Age | 0.181 | 0.2 | 0.147 | 0.4 | 0.152 | 0.06 | 0.046 | 0.7 |
| Sex | 0.233 | 0.1 | 0.169 | 0.2 | -0.154 | 0.2 | 0.121 | 0.2 |
| Physical exercise | 0.109 | 0.3 | -0.046 | 0.6 | -0.168 | 0.2 | 0.203 | 0.6 |
| HIV + since 1st diagnosis | 0.090 | 0.4 | 0.108 | 0.04 | -0.075 | 0.9 | 0.150 | 0.1 |
| HAART | 0.055 | 0.3 | 0.015 | 0.06 | -0.087 | 0.7 | 0.202 | 0.06 |
| Duration on EFV | 0.146 | 0.2 | 0.038 | 0.9 | 0.002 | 0.6 | 0.022 | 0.8 |
| CD4 count | 0.082 | 0.5 | 0.004 | 0.8 | 0.130 | 0.06 | 0.004 | 0.8 |
| Female anthropometric indicators | | | | | | | | |
| Waist circumference | 0.315 | 0.02 | 0.249 | 0.06 | -0.020 | 0.8 | 0.248 | 0.07 |
| Waist-hip ratio | 0.201 | 0.1 | 0.313 | 0.02 | 0.114 | 0.4 | 0.244 | 0.07 |
| Body mass index | 0.473 | 0.001 | 0.430 | 0.001 | -0.011 | 0.9 | 0.250 | 0.06 |
| Male anthropometric indicators | | | | | | | | |
| Waist circumference | 0.030 | 0.9 | 0.026 | 0.8 | -0.271 | 0.1 | -0.145 | 0.4 |
| Waist-hip ratio | 0.211 | 0.2 | 0.170 | 0.3 | 0.097 | 0.6 | 0.086 | 0.6 |
| Body mass index | -0.003 | 0.9 | -0.096 | 0.6 | -0.309 | 0.07 | -0.002 | 0.9 |

Key: r= Pearson correlation coefficient, p= p value for Pearson correlation, ρ = Spearman Rank Correlation Coefficient, P = p-value for Spearman correlation, TC =Total Cholesterol, TG= Triglyceride, LDL-C= Low Density Lipoprotein-Cholesterol, HDL-C= High Density Lipoprotein-Cholesterol, HIV= Human Immune Deficiency Syndrome Virus, HAART= Highly Active Anti Retroviral Therapy, CD4= Cluster of Differentiation, EFV= Efavirenz

# Figures

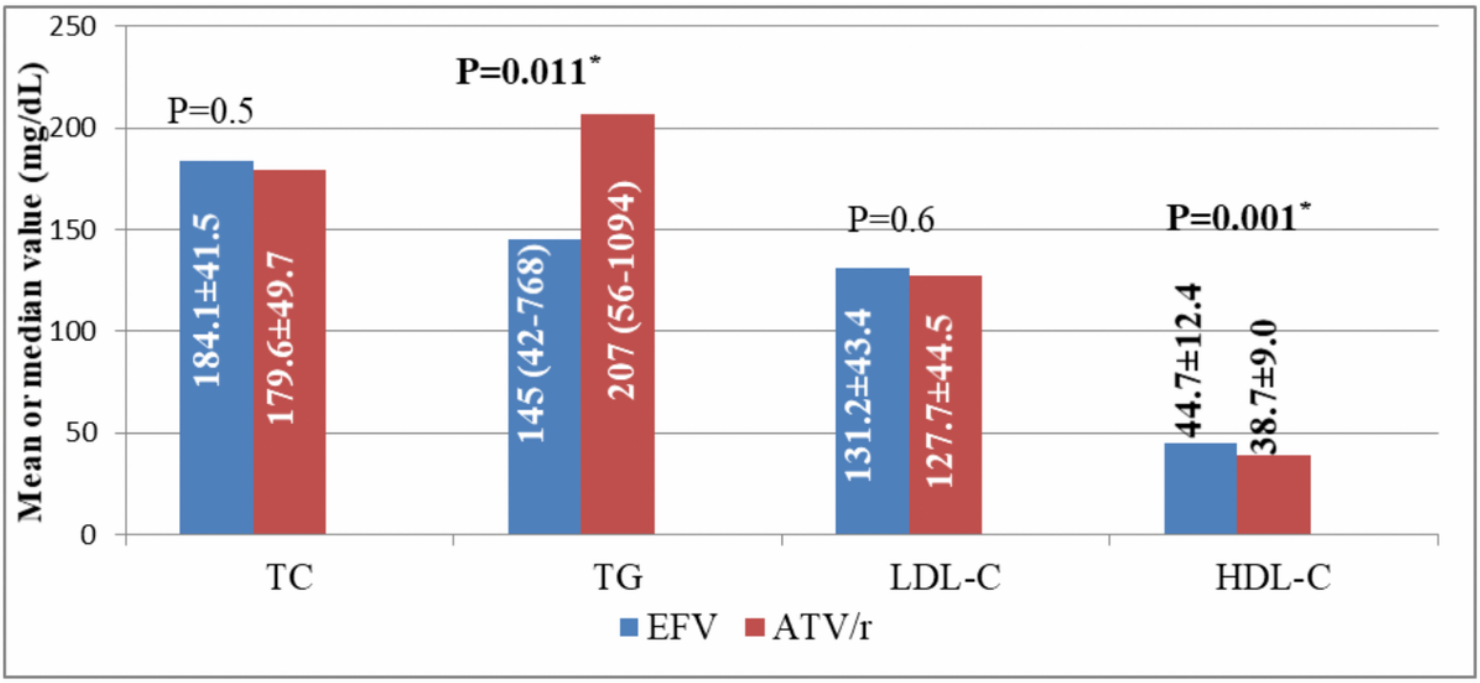


**Figure 1**

Comparisons of mean of lipid parameters between EFV and ATV/r-treated patients. Legends: TC= Total Cholesterol, TG=Triglyceride, LDL-C= Low Density Lipoprotein-Cholesterol, HDL-C =High Density Lipoprotein-Cholesterol, *= statistical significance, continuous variables are presented as mean ± SD for TC, LDL-C and HDL-C and median (IQR) for TG. IQR=Inter Quartile Range, SD= Standard Deviation

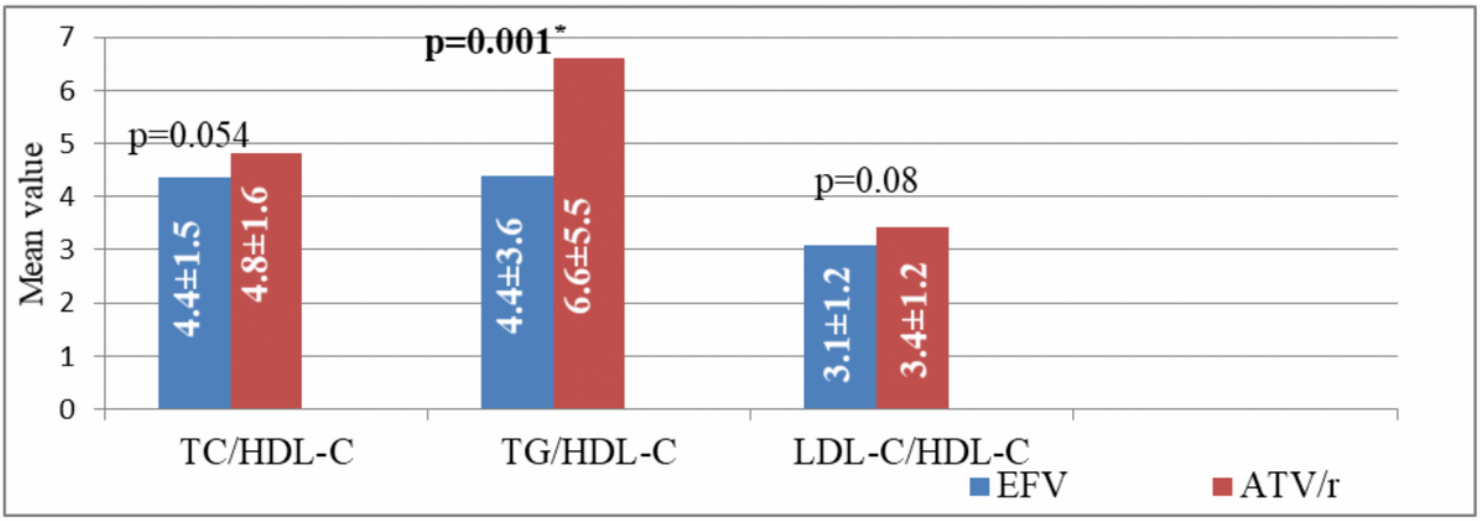


**Figure 2**

Comparisons of mean values of lipid ratios between EFV- and ATV/- treated patients Legends: TC/HDL-C= Total Cholesterol/High Density Lipoprotein-Cholesterol, TG/HDL-C= Triglyceride/ High Density Lipoprotein-Cholesterol, LDL-C/HDL-C= Low Density Lipoprotein-Cholesterol/ High Density Lipoprotein-Cholesterol, EFV Efavirenz, ATV/r= Ritonavir-boosted atazanavir