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Full Length Research Paper

Change in serum lipid profiles and glucose subsequent to changing from stavudine/lamivudine to zidovudine/lamivudine in non-nucleoside reverse transcriptase inhibitors based hostile to retroviral regimens in Southern Ethiopia

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Data concerning any difference in serum lipid profiles and glucose level after patients switched from stavudine to zidovudine in Ethiopia is very limited. Seventy eight adults receiving antiretroviral therapy (ART) that included stavudine/lamivudine with either of efavirenz or nevirapine during ART initiation were enrolled. Of these patients, 53 were switched to zidovudine/lamivudine/nevirapine (NVP-group) and the rest 25 were switched to zidovudine/lamivudine/efavirenz (EFV-group). Serum lipid profiles and glucose were determined after overnight fasting. Dyslipidemia and dysglycaemia were assessed according to the United State National Cholesterol Education program-III guideline. Statistical analysis was done using Statistical Package for Social Sciences (SPSS) Version 20. Of the 78 patients, 39.7% were males and 60.3% were females. At the end of the study follow-up, the prevalence of TC ≥ 200 mg/dl, LDL-c ≥ 130 mg/dl, TG ≥ 150 mg/dl, HDL-c < 40 mg/dl and glucose ≥ 110 mg/dl were higher in EFV group when compared with NVP. About 74.4% patients had at least two laboratory abnormities which is compatible with a diagnosis of dyslipidemia at 12 month of post switch. Four lipid profiles abnormal within a single individual was 16% in EFV and 3.8% in NVP group, p = 0.08. Raised HDL-c concentration was observed in NVP group in both periods when compared with EFV. In addition, patients that switched from d4T/3TC/NVP to AZT/3TC/NVP had a significant change in TC and TG (p = 0.001 for both). Also TC ≥ 200 mg/dl was decreased from 49 to 16% (p = 0.04). Furthermore, sex was significantly and negatively associated with raised TC and TGs among patients using NVP based regimen. Raised HDL-c concentration, decreased proportion of abnormal lipid profiles and abnormal glucose was observed in the NVP group. Based on these findings, NVP may be expected to reduce the risk of cardiovascular diseases.

Key words: Dyslipidemia, dysglycaemia, human immunodeficiency virus/acquired immune deficiency syndrome (HIV/AIDS), antiretroviral therapy, Ethiopia.

INTRODUCTION

Highly active antiretroviral therapy (HAART) has effectively reduced morbidity and mortality among patients living with human immunodeficiency virus (HIV) infection (Grinspoon et al., 2005; John et al., 2001). In

addition, HAART also has a potential to significantly reduce the risk of HIV transmission and the spread of tuberculosis (UNAIDS, 2013). Since its introduction, patients have started to live longer, however co-morbid problems have been emerged. Among these challenges, lipid profile derangements, insulin resistance, and diabetes are some of the metabolic complications of long-term use of HAART (Cohan, 2000; DAD, 2003). Dyslipidemia in HIV-infected patients using HAART includes, elevated level of total cholesterol (TC), LDL cholesterol (LDL-c), triglycerides (TG), and decreased HDL-cholesterol (HDL-c), and severe hypertriglyceridemia in several patients (El-Sadr et al., 2005). Stavudine (d4T) from nucleoside reverse transcriptase inhibitors (NRTIs) regimens is the most commonly mentioned antiretroviral agent that is being associated with metabolic syndrome (MS) and HIV related fat accumulation (Matinez et al., 2004; Jemsek et al., 2006). Lipoatrophy and lipohypertrophy are associated with multiple metabolic derangements in the setting of HIV infection and antiretroviral therapy (ART). In addition, visceral adipose tissue (VAT) has been linked to CVD in HIV-infected men irrespective of BMI or waist girth (Haubrich et al., 2009). The protease inhibitors (PIs) in general have been reported to be highly associated with MS (Cerrato et al., 2012). However, non nucleoside reverse transcriptase inhibitors (NNRTIs) based regimens importantly differ from PI-based regimens by being associated with marked increases of HDL-c and slighter raises of LDL-c and TGs (Van der Valk et al., 2001; Tashima et al., 2003). Furthermore dyslipidemia like hypertriglyceridemia, low level of HDL-c and insulin resistance can occur concurrently in HIV infection, which eventually raises the risk of cardiovascular disease (CVD) (Pao et al., 2008).

Following the recommendations from WHO 2010 guidelines, 2013 d4T was phased-out in Ethiopia from adults' treatment option, due to its metabolic toxicity than other NRTIs (WHO, 2010). The replacing of d4T + lamivudine (3TC) with zidovudine (AZT) + 3TC is not as a result of immunological failure but for the risks of metabolic and anthropometric alterations in HIV-infected patients. Therefore, this cohort study was designed to examine the effect of regimens substitution in lipid profiles, serum glucose and cardiovascular risks after 12 month of post switch, in a resource limited setting.

METHODOLOGY

Study setting and population

This prospective cohort study was carried out from May 2013 to July 2014 at ART clinic of Hawassa University Teaching Referral Hospital. Eligible patients were HIV -infected, immunologically stable adults and initial NRTI backbone was d4T+3TC with one of the NNRTI (either EFV or NVP). The inclusion criteria for this sub study were the patients who had continued with their initial antiretroviral regimens for a minimum of two years of treatment. Any patient who had changed antiretroviral drug in the initial regimen due to any reason before current switching was excluded. All recruited patients were those patients that switched from d4T+3TC to AZT+3TC without changing NNRTI-based regimens. All participants were ≥18 years of age, and have a good ART adherence (adherence rate ≥95%). A good adherence is defined by missing <2 dose of 30 doses or <3 dose of 60 doses; and it was adopted from Ethiopian Federal Ministry of Health (FMOH), HIV Care/ART follow-up form. Participants receiving statin drugs, pregnant women, known diabetes mellitus patients, patients who took alcohol within 24 h and renal failures were excluded. Subjects were monitored at the time of switching (month 0) and 12 month subsequently for serum lipid profiles and glucose analysis.

For all participants, data were collected on the socio-demographic information together with body mass index, medical history including diabetes mellitus, renal failures and use of drugs that alter lipid profiles. CD4+ lymphocyte count was done by K_2EDTA anticoagulated blood using flow cytometry instrument (Becton Dickinson, CA, USA). After an overnight fast of 8 to 12 h, venous blood was collected in plain tube from each patient and it was centrifuged within 15 to 20 min of collection at 3000 cycles/min for 5 min. Then serum was separated immediately for determination of serum glucose and lipid profiles (TC, HDL-c, LDL-c and TGs) using A25 Random Access Analyzer (BioSystems^{TM}, Spain). Serum glucose level was measured by the glucose oxidase method (GOD-PAP). Enzymatic colorimetric assay method was used for the measurement of TC (CHOD-PAP method) and TG (GPO-PAP method) while direct homogeneous enzymatic colorimetric assay technique was used for the measurement of HDL-c and LDL-c. The required reagents for all these tests were from Human Gesellschaft für Biochemica und Diagnostica mBH (Germany).

Finally, lipid profile derangements was defined as TC ≥200 mg/dl, HDL-c <40 mg/dl, LDL-c ≥130 mg/dl and TG ≥150 mg/dl, while a fasting glucose level ≥110 mg/dl for dysglycaemia according to the United States National Cholesterol Education Program, Adult Treatment Panel (NCEP-ATP) III guidelines (NCEP-III, 2002). To assess cardiovascular risk, Castelli's Index I was calculated, TC/HDL-c ratio: a Castelli's Index I >5.1 for men and >4.4 for women were considered indicative of an elevated CVD risk (Castelli et al., 1983).

Statistical analysis

Analysis included for all participants showing as a minimum of one visit after initiating AZT. Mean (± standard deviation, SD), median (interquartile range at 25 and 75th, IQR) and frequencies were used to describe patients' characteristic as appropriate. Chi-square test and Mann-Whitney U test were used to compare categorical and continuous variables between the two treatment groups (EFV vs. NVP). Pair-samples T test were used to compare measures between the switch baseline and at 12 months after initiating AZT. The independent variables were evaluated with logistic regression to identify the factors that were associated with abnormal lipid profile and glucose. P-value less than 0.05 was considered as statistically significant at 95% confidence interval (CI).

Ethical clearance

The study was approved by Institutional Review Board (IRB) of Hawassa University College of Medicine and Health Science. Written informed consent was obtained from all participants.

RESULTS

General characteristics of study participants

A total of 80 HIV-infected patients met the inclusion criteria of this study; however, 78 patients (males 31 (39.7%), females 47(60.3%)) were followed until the end of this study. Data from patients who were lost to follow-up were not included in this analysis. Patients switched from the d4T/3TC/EFV to AZT/3TC/EFV and from d4T/3TC/NVP to AZT/3TC/NVP at the time of regimen substitutions. Of the 78 patients, 25 (32%) were in the AZT/3TC/EFV group and 53 (68%) were in the AZT/3TC/NVP group. Baseline age of the individuals was 40.9 months with standard deviation of 7.8. There was a significant differences in age ≥40 years, in CD4+ T-lymphocyte categories and duration of HAART experiences in between NNRTI groups, p=<0.05. However, median CD4+ cells count and the rest demographic characteristics were not significantly different from the switch baseline (0 month) in between NNRTIs, p ≥ 0.05 (Table 1).

Characteristics of the lipid profiles and glucose abnormalities at the switched 0 month

Lipid profile tests (TC, TG, HDL-c, and LDL-c), and glucose were performed for a total of 78 participants. The mean TC, and TC/HDL- c ratio were higher among patients using NVP based regimen when compared with patients using EFV, but not significant. The median (IQR) of TG/HDL-c ratio was 4.3 (3.0 to 10.6) in EFV group and 4.4 (2.6 to 6.9) in NVP group (p=0.52). TG/HDL-c ratio (≥2.4), is an indicator of insulin resistance disorder, which was 84% in EFV group and 81% in NVP group (p=0.76). The mean LDL-c and median value of TG was insignificantly higher in EFV group when compared with NVP group (Table 1) . Also, the prevalence of lipid profiles TC ≥ 200 mg/dl and TG ≥150 mg/dl were higher in NVP group when compared with EFV group, but the difference was not significant.

Moreover, the prevalence of HDL-c is below 40 mg/dl, glucose ≥110 mg/dl Castelli's index I and LDL-c ≥130 mg/dl were higher in EFV group when compared with those on NVP (Table 1). Derangement of four lipid profiles within a single individual (TC, TG, HDL-c, LDL-c) according to NCEP-ATP III was 12% in EFV group and 15.1% in NVP group, (p=0.71). The proportion of patients with serum glucose level >180 mg/dl were 12% in EFV group whereas 3.7% in NVP group.

Characteristics of lipid profiles and glucose after 12 month of AZT/3TC replacement

The mean TC, TC/HDL-c ratio, LDL-c, glucose and median TG were higher among patients using EFV when compared with patients using NVP, but not significant. However, the mean HDL-c value was higher among patients using NVP when compared with those using EFV (Figure 1).

In addition, the prevalence of TC ≥200 mg/dl, LDL-c ≥130 mg/dl, TG ≥150 mg/dl, HDL-c <40 mg/dl, Castelli's index I and glucose ≥110 mg/dl, were insignificantly higher in EFV group when compared with those on NVP (Figure 2). About 74.4% patients had at least two lipid profile laboratory abnormalities, which is compatible with a diagnosis of dyslipidemia. However, derangement of four lipid profiles within a single individual was higher in EFV group (16%) when compared with NVP group (3.8%), p=0.08. The prevalence of patients with serum glucose level >180 mg/dl was 8.0% in EFV group, whereas 7.5% in NVP. Furthermore, the percentage change of parameters between EFV versus NVP is depicted as shown in Table 2.

Lipid profiles and glucose between switch 0 month versus 12 month of post switch within the same NNRTI based regimen

Patients switched from d4T/3TC/EFV to AZT/3TC/EFV showed insignificant differences in mean and median value of lipid profiles (TC, TG, LDL-c and TC/HDL-c ratio), p≥0.05. The proportions of TC ≥ 200 mg/dl, TG ≥150 mg/dl, HDL-c <40 mg/dl, Castelli's index I and glucose ≥110 were increased at the 12 month of post switch. In contrast, those patients switched from d4T/3TC/NVP to AZT/3TC/NVP showed a significant decrease in mean TC and median TG (p = 0.001 for both), and also TC ≥200 was significantly decreased from 49 to 16% (p=0.04). Moreover, the proportion of Catelli's index I, an indicator of the cardiovascular diseases risk, was decreased from 33.9 to 28.3% (Table 3).

Univariate and multivariate analysis were applied to assess possible predicted factors associated with each abnormal lipid profile among patients within NVP regimen. In both models, sex was significantly and negatively the associated risk factor of raised TC and TGs (Table 4).

DISCUSSION

The aim of this cohort study carried out in a resource limited setting was to assess the trend of lipid profile derangements and dysglycaemia among HIV-infected patients switched from d4T/3TC to AZT/3TC based regimens without changing NNRTIs. Most HAART drugs have been found to induce moderate to severe toxic

Table 1. Baseline characteristics at the time of NRTI switching (month 0) in between EFV versus NVP.

Variable	Total	EFV	NVP	p value
	n (%)			
Gender				
Male	31 (39.7)	11 (44.0)	20 (37.7)	0.62
Female	47 (60.3)	14 (56.0)	33 (62.3)	
Age (years), mean ±SD	40.9 (7.8)	42.2 (7.3)	40.3 (8.1)	0.34
20-30	4 (5.1)	1(4.0)	3(5.7)	-
31-40	35 (44.9)	8 (32.0)	27(50.9)	-
41-50	29 (37.2)	12(48.0)	17(32.1)	-
>50	10 (12.8)	4 (16.0)	6 (11.3)	0.40
≥40	41 (52.6)	18(72.0)	23(43.4)	0.01
BMI (kg/m^2), mean ±SD	22 (2.9)	22.1 (2.9)	21.9 (2.9)	0.70
≥25 kg/m^2,	12 (15.4)	4 (16.0)	8 (15.1)	0.91
CD4+ count (cells/mm^3)*	581 (443-848)	560 (445-917)	583 (405-834)	0.47
<350	13 (16.7)	1(4.0)	12(22.6)	-
350-500	16 (20.5)	9 (36.0)	7 (13.2)	-
>500	49 (62.8%)	15(60.0)	34(64.2)	0.01
HAART experience (month), mean ±SD	62 (16)	65.5 (11)	60.2 (17.6)	0.09
24-48	14 (17.9)	1(4.0)	13(24.5)	-
49-72	48 (61.5)	20 (80)	28(52.8)	-
≥73	16 (20.5)	4 (16.0)	12(22.6)	0.04
TC (mg/dl), mean ±SD	202 (68)	193 (50)	206 (75)	0.46
≥200mg/dl	36 (46.2)	10(40.0)	26(49.1)	0.45
TG (mg/dl)*	194 (132-379)	206 (124-439)	187 (134-365)	0.82
≥150 mg/dl	49 (62.8)	15(60.0)	34(64.2)	0.72
HDL-cholesterol (mg/dl), mean ±SD	47 (11)	44.6 (8.8)	48.4 (11.8)	0.14
<40 mg/dl	17 (21.8)	6 (24.0)	11(20.7)	0.74
LDL-cholesterol (mg/dl), mean ±SD	107 (44)	109.4 (36)	106.5 (48)	0.50
≥130 mg	24 (30.8)	9 (36.0)	15(28.3)	0.49
Glucose (mg/dl), mean ±SD	125 (46)	138 (65.6)	118.8 (32)	0.07
≥110 mg/dl	35 (44.9)	14(56.0)	21 (39.6	0.17
TC/HDL-cholesterol ratio, mean ±SD	4.4 (1.5)	4.5 (1.4)	4.4 (1.6)	0.82
Castelli's Index I	29 (37.2)	11(44.0)	18(33.6)	0.39

TC: Total cholesterol; HDL: high-density lipoprotein; LDL: low-density lipoprotein; SD: standard deviation; BMI: body mass index; TG: triglyceride; EFV: Efavirenz; NVP: Nevirapine; HAART: highly active antiretroviral therapy; Castelli's Index I (TC/HDL-c ratio) for females >4.4 and males >5.1; *values in median with interquartile range

effects after long-term use and therefore pose a tackle to chemotherapy (Sharma, 2011). Patients are switched to a new regimen because of the adverse effects of d4T therapy, but not due to immunological failure. It was found that the CD4+ cells count in the EFV group was not significantly different from the NVP group, thus shows the EFV is similar in immunological properties in HIV-infected patients when compared with NVP.

In the present study, majority of the patients (74.4%) had at least two laboratory abnormalities, which is compatible with a diagnosis of dyslipidemia according to NCEP-ATP III criteria at the end of the study follow-up. HIV-1 infection itself or use of HAART may induce oxidative stress and it predisposes for further pathogenesis in HIV infected patients (Sharma, 2014). The association between dyslipidemia and HAART has been mainly described for PIs based regimens (Anastos et al., 2007; Nery et al., 2011). Lipid derangements were higher among patients who received d4T when compared with other NRTIs (Kalyanasundaram et al., 2012; Ceccato et al., 2011). NNRTIs derange lipid profiles during therapy (Van der Valk et al., 2001; Young et al., 2005); however, evidences in support of the characteri-zation of dyslipidemia regarding NNRTIs after HAART switching in sub-Saharan African countries are scarce. Similar with our findings: a cohort study report from

Table 2. Mean percentage change of parameters in between NNRTIs after 12 months.

Parameter	NNRI	Mean (Switch 0 month)	Mean % change	Std. error of mean	P value	95% Confidence interval of the difference	
						Lower	Upper
TC	EFV	193	4.1464	5.8	0.028	1.31724	22.91010
	NVP	206	-7.9672	2.5			
TG	EFV	206	4.4214	12.2	0.09	-3.23656	41.87073
	NVP	187	-14.8957	5.2			
HDL	EFV	44.6	0.7313	7.2	0.70	-22.28461	15.17561
	NVP	48.0	4.2858	5.4			
LDL	EFV	109	2.3587	6.1	0.96	-16.85793	16.20562
	NVP	106.6	2.6848	4.9			
TC/HDL-c	EFV	4.4	14.6798	9.2	0.046	.35638	35.38215
	NVP	4.4	-3.1894	4.2			
Glucose	EFV	138.6	-14.1502	5.6	0.25	-26.21232	6.96721
	NVP	119	-4.5276	5.0			
TG/HDL-c	EFV	8.4	-80.7608	4.1	0.43	-5.21640	11.94757
	NVP	6.9	-84.1264	2.2			

TC: Total cholesterol; HDL: high-density lipoprotein; LDL: low-density lipoprotein; SD: standard deviation; TG: triglyceride; EFV: Efavirenz; NVP: Nevirapine. Mean percentage change was calculated for each individual patient as ((concentration [12 month after ART switch] – concentration [switch baseline]) / concentration [switch baseline]) ×100, was adopted from van Leth F et al. (2004).

Germany revealed that a substitution of d4T with other NRTIs may reverse lipid derangements (Claas et al., 2007).

It was found out that the proportions of TC ≥200 mg/dl, TG ≥150 mg/dl, LDL-c ≥130 mg/dl, TC/HDL-c ratio and HDL-c <40 mg/dl were higher in EFV group (48, 76, 32, 48 and 32%) when compared with NVP group (30.2, 62.3, 24.5, 28.3 and 30.2%), respectively. These described abnormal lipid profiles in EFV group are atherogenic (NCEP-III, 2002; Asztalos et al., 2006; Sudano et al., 2006), and suggest a potential risk for the development of cardiovascular diseases in a significant proportion among HIV-infected patients in the near future. The randomized trial report of 2 non-nucleosides (2NN) indicated that patients on NVP group had significantly improved HDL-c concentration and had relatively low lipid profile derangements when compared with those on EFV (van Leth et al., 2004). Also, the finding of the present study indicates HDL-c concentration was slightly higher in the NVP group when compared with EFV, hence it confirms that ART regimen which contains NVP has anti-atherogenic effects (Van der Valk et al., 2001; van Leth et al., 2004), in addition to restoration of patients' health.

Furthermore, the trends of lipid profile within a single group (EFV in NRTI switch 0 month versus EFV at the 12 month of post switch; and NVP in NRTI switch 0 month versus NVP at the 12 month of post switch) was checked. Patients in the EFV group had raised TC/HDL-c, TG, TC and TC/HDL-c when compared with the switch baseline. However, a significant decreasing trend was observed in the mean TC, median TG and TC ≥200 mg/dl in NVP group at the end of the study follow-up when compared with EFV. Similarly, it has been stated that EFV has a deleterious effect on lipids when compared with NVP (Erdembileg et al., 2009; Tungsiripat et al., 2005). These variations may be due to patient characteristics such as life style, gender and race/ethnicity, drug metabolism polymorphism which affect differences in lipid profile between populations taking the same antiretroviral drug (Armstrong et al., 2011). Also treatment duration may contribute to these differences (Tomazic et al., 2004; Jevtovic et al., 2009).

In the present study, univariable and multivariable analysis were applied to assess possible predicted factors associated with each abnormal lipid profile among patients within NVP group. In both models, sex was a significantly and negatively associated risk factor for raised TC and TGs; but the findings are not in line with the cross-sectional study conducted in Cameroon (Pefura Yone et al., 2011).

Table 3. Comparison of parameters between switch baseline and 12 months with in a group.

Variable	EFV	EFV	P value	NVP	NVP	P value
	Month (0)	Month 12		Month (0)	Month 12	
TC (mg/dl)*	193 (50)	193.6 (46)	0.97	206 (75)	183 (51)	0.001
TG (mg/dl)#	206 (124-439)	221(143-274)	0.06	187 (134-365)	181 (97-250)	0.001
HDL-c (mg/dl)*	44.6 (8.9)	44 (15)	0.85	48 (11.8)	48.7 (16.3)	0.89
LDL-c (mg/dl)*	109 (36)	106 (34.5)	0.60	106.6 (48)	106 (34.9)	0.19
TC/HDL-c ratio*	4.4 (1.4)	4.8 (1.7)	0.34	4.4 (1.6)	3.9 (1.2)	0.11
Glucose (mg/dl)*	138.6 (65)	117 (68)	0.07	119 (32)	109.5 (40)	0.16
CD4+ cells/mm^3*	560 (445-917)	580 (494-967)	0.49	583 (405-834)	551 (361-767)	0.27
TC ≥ 200 (mg/dl)**	10 (40.0)	12 (48.0)	0.56	26 (49.0)	16 (30.2)	0.04
TG ≥ 150 (mg/dl)**	15 (60.0)	19 (76.0)	0.22	34 (64.1)	33 (62.2)	0.84
HDL-c< 40 (mg/dl)**	6 (24.0)	8 (32.0)	0.52	11 (20.7)	16 (30.2)	0.26
LDL-c ≥130 (mg/dl)**	9 (36.0)	8 (32.0)	0.76	15 (28.3)	13 (24.5)	0.65
Glucose ≥110 (mg/dl)**	14 (56.0)	9 (36.0)	0.15	21 (39.6)	14 (26.4)	0.14
Castelli's Index I**	11 (44.0)	12(48.0)	0.77	18 (33.9)	15 (28.3)	0.52

TC: Total cholesterol; HDL-c: high -density lipoprotein cholesterol; LDL-c: low-density lipoprotein cholesterol; SD: standard deviation; TG: triglyceride; EFV: Efavirenz; NVP: Nevirapine; Castelli's Index I (TC/HDL-c ratio) for females >4.4 and males >5.1; *Values in mean with standard deviation; **Values in number with percentage; #Values in median with interquartile range; Month (0), switch baseline.

Table 4. Determinants of abnormal lipid profiles in the NVP group at the 12 month of NRTI switch.

Outcome variable	Explanatory variable	Unadjusted odds ratio	95%CI	P value	Adjusted odds ratio	95%CI	P value
TC≥200 mg/dl	Sex	0.15	0.03-0.76	0.02	0.14	0.02-0.88	0.03
	Age	0.48	0.14-1.65	0.24	1.05	0.25-4.56	0.94
	BMI	0.73	0.13-4.12	0.73	0.89	0.13-6.09	0.91
	CD4+ count	1.27	0.38-4.22	0.69	1.02	0.27-3.84	0.98
	HAART	0.96	0.25-3.70	0.95	0.88	0.20-3.83	0.86
TG≥150mg/dl	Sex	0.09	0.18-46	0.004	12.76	2.01-80.99	0.007
	Age	2.47	0.76-8.00	0.13	0.98	0.22-4.35	0.98
	BMI	1.00	0.21-4.78	0.98	0.84	0.12-5.93	0.86
	CD4+ count	0.79	0.26-2.44	0.79	1.87	0.48-7.23	0.36
	HAART	0.96	0.26-3.48	0.95	1.22	0.28-5.37	0.79

TC: Total cholesterol; TG: triglyceride; HAART:highly active antiretroviral therapy; BMI: body mass index. BMI <25 kg/m^2; Females, Age ≤ 40 years, CD4+ count ≥500 cells/mm^3, HAART experience >48 months

Antiretroviral-specific risk factors for glucose abnormalities include the exposure to PIs and to certain NRTIs. Of these, the use of PIs has emerged as the strongest risk factor, with studies from the early HAART era suggesting a prevalence of 8 to 46% for the spectrum of glucose metabolism abnormalities, which includes, impaired glucose tolerance, insulin resistance and diabetes in patients receiving PIs (Behrens et al., 1999; Mauss et al., 1999). The present study finding indicated no significant differences between EFV and NVP regarding glucose abnormality (≥110 mg/dl); however, the abnormal rate was decreased in both groups after 12 months of post switch. A substitution of d4T to AZT may reverse lipid derangements and it may provide a good opportunity to improve dysregulation of glucose in HIV-treated patients. A high TG/HDL-C ratio ≥2.4 is a strong indicator of the insulin resistance syndrome (NCEP-III, 2002; Einhorn et al., 2003; McLaughlin et al., 2003), which was higher in EFV group when compared with NVP but not significant (84% versus 71.7%; p=0.27). So, a wide-ranging analysis of the accessible literature on the toxicity of ARV drugs, their mechanisms of action and possible management strategies are mandatory to combat such complications (Sharma, 2011).

Conclusion

Our study indicates a decreased proportion of abnormal

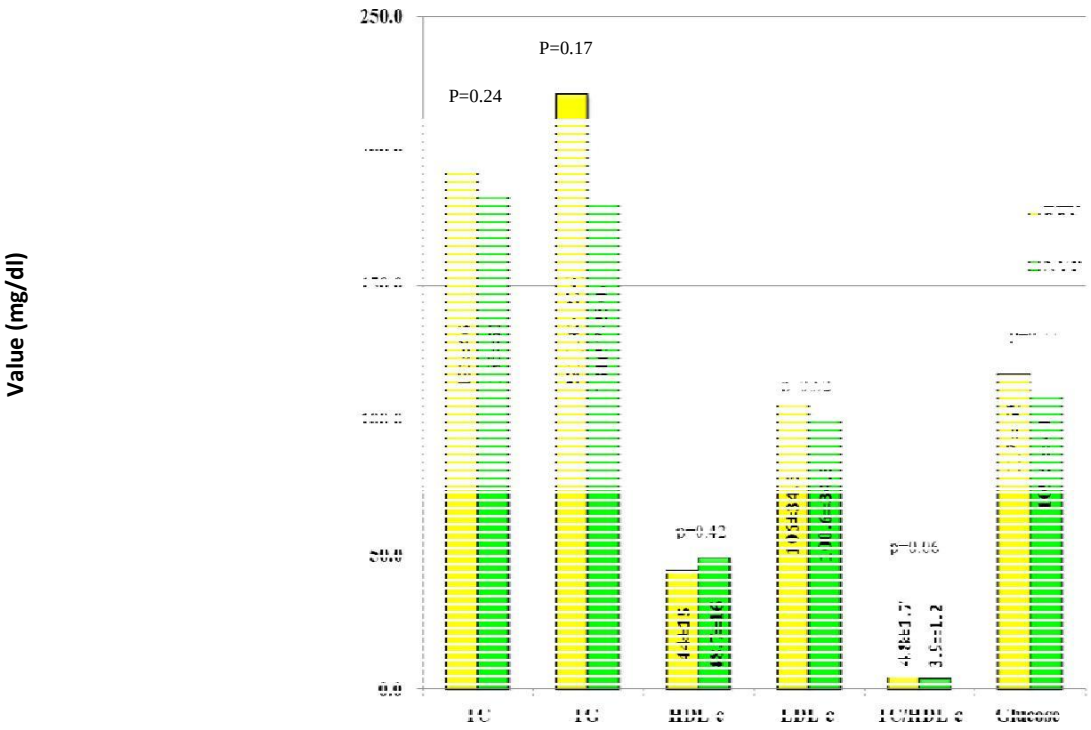

Figure 1. Comparing of mean (standard deviation) and median (interquartile range) measures between EFV vs. NVP groups at the 12 month of NRTI switching.

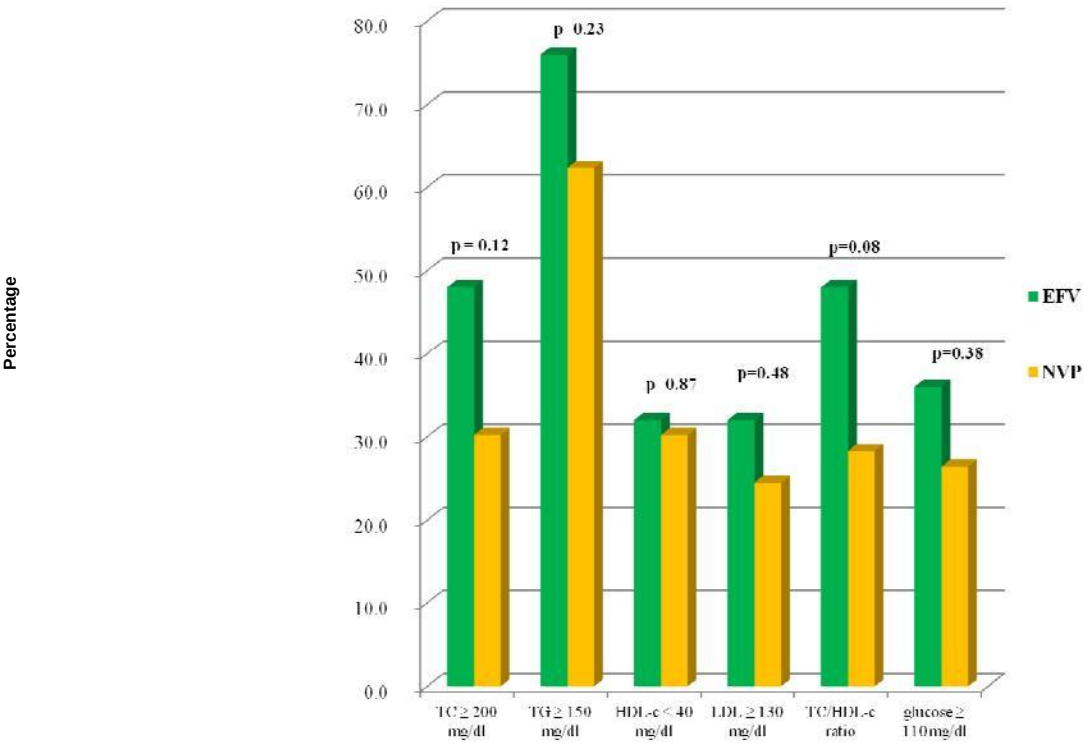

Figure 2. Comparisons of lipid profile derangements and dysglycaemia in the EFV versus NVP group at the 12 month of NRTI switching according to NCEP-ATP III.

TC, TG, HDL-c, LDL-c, TC/HDL-c ratio and glucose among patients using NVP when compared with EFV at the end of the study follow-up according to NCEP-ATP III. Also raised HDL-c was seen in NVP group. Based on these findings, HAART regimens which contain NVP may be expected to reduce the risk of cardiovascular diseases. Therefore, it is recommended that lipid profiles should be monitored periodically for the maximum benefit of patients' health management.

Abbreviations: 2NN, 2 Non-nucleosides; **AIDS,** acquired immunodeficiency syndrome; **HAART,** highly active antiretroviral therapy; **3TC,** lamivudine; **HIV,** human immunodeficiency virus; **AZT,** zidovudine; **d4T,** stavudine; **EFV,** efavirenz; **ART,** antiretroviral therapy; **HDL-c,** HDL-cholesterol; **LDL-c,** LDL-cholesterol; **NNRTIs,** non-nucleoside reverse transcriptase inhibitors; **NVP,** nevirapine; **PIs,** protease inhibitors; **TC,** total cholesterol; **TG,** triglycerides; **SPSS,** Statistical Package for Social Sciences; **NCEP-ATP,** United States National Cholesterol Education Program, Adult Treatment Panel.

Conflict of interest

The authors declare no competing interests.

REFERENCES

Anastos K, Lu D, Shi Q, Tien PC, Kaplan RC, Hessol NA, Cole S, Vigen C, Cohen M, Young M, Tien, Phyllis C, Vigen C, Justman J (2007). Association of serum lipid levels with HIV sero-status, specific antiretroviral agents and treatment regimens. J. Acquir. Immune Defic. Syndr. 45(1):34-42.

Armstrong C, Liu E, Okuma J, Spiegelman D, Guerino C, Njelekela M, Grinspoon S, Fawzi W, Hawkins C (2011). Dyslipidemia in an HIV-positive antiretroviral treatment-naive population in Dar es Salaam, Tanzania. J. Acquir. Immune Defic. Syndr. 57(2):141-145.

Asztalos BF, Schaefer EJ, Horvath KV, Cox CE, Skinner S, Gerrior J, Gorbach SL, Christine Wanke C (2006). Protease inhibitor-based HAART, HDL, and CHD-risk in HIV-infected patients. Atherosclerosis 184(1):72-7.

Behrens G, Dejam A, Schmidt H, Balks HJ, Brabant G, Körner T, Stoll M, Schmidt RE (1999). Impaired glucose tolerance, beta cell function and lipid metabolism in HIV patients under treatment with protease inhibitors. AIDS 13(10):63-70.

Castelli WP, Abbott RD, McNamara PM (1983). Summary estimates of cholesterol used to predict coronary heart disease. Circulation 67(4):730-4.

Ceccato M, Bonolo P, Souza Neto A, Araújo F, Freitas M (2011). Antiretroviral therapy-associated dyslipidemia in patients from a reference center in Brazil. Braz. J. Med. Biol. Res. 44(11):1177-83.

Cerrato E, Ascenzo F, Binodi-Zoccai G, Omede P, Moretti C, Cicalini S, Parthasarathi G, Sheiban I, Gaita F (2012). Acute coronary syndrome in HIV patients: from pathophysiology to clinical practice. Cardiovasc. Diagn. Ther. 2(1):50-55.

Claas GJ, Julg B, Roling J, Goebel FD, Bogner JR (2007). Metabolic and anthropometric changes one year after switching from didanosine/stavudine to tenofovir in HIV-infected patients. Eur. J. Med. Res. 12:54-60.

Cohan GR (2000). HIV-associated metabolic and morphologic abnormality syndrome: Welcome therapy may have unwelcome effects. Postgrad. Med. 107(4):141-46.

Einhorn D, Reaven GM, Cobin RH, Ford E, Ganda OP, Handelsman Y, Hellman R, Jellinger PS, Kendall D, Krauss RM, Neufeld ND, Petak SM, Rodbard HW, Seibel JA, Smith DA, Wilson PW (2003) . American college of Endocrinology position statement on the insulin resistance syndrome. Endocr. Pract. 9(3):237-52.

El-Sadr W, Mullin C, Carr A, Gibert C, Rappoport C, Visnegarwala F, Grunfeld C, Raghavan S (2005). Effects of HIV disease on lipid, glucose and insulin levels: results from a large antiretroviral-naïve cohort. HIV Med. 6(2):114-21.

Erdembileg A, Alison S, Lars B (2009). Human Immunodeficiency Virus and Highly Active Antiretroviral Therapy-Associated Metabolic Disorders and Risk Factors for Cardiovascular Disease. Metab. Syndr. Relat. Disord. 7(5):401-409.

Grinspoon S, Carr A (2005). Cardiovascular risk and body-fat abnormalities in HIV-infected adults. N. Engl. J. Med. 352(1):48-62.

Haubrich RH, Riddler SA, Dirienzo AG, Komarow L, Powderly WG, Klingman K, Garren KW, Butcher DL, Rooney JF, Haas DW, Mellors JW, Havlir DV (2009). Metabolic outcomes in a randomized trial of nucleoside, nonnucleoside and protease inhibitor-sparing regimens for initial HIV treatment. AIDS 23(9):1109-18.

Jemsek JG, Arathoon E, Arlotti M, Perez C, Sosa N, Pokrovskiy V, Thiry A, Soccodato M, Noor MA, Giordano M (2006). Body fat and other metabolic effects of atazanavir and efavirenz, each administered in combination with zidovudine plus lamivudine, in antiretroviral-naive HIV infected patients. Clin. Infect. Dis. 42(2):273-80.

Jevtovic DJ, Dragovic G, Salemovic D, Ranin J, Djurkovic- Djakovic O (2009). The metabolic syndrome, an epidemic among HIV-infected patients on HAART. Biomed Pharmacother. 63(5):337-42.

John M, Nolan D, Mallal S (2001). Antiretroviral therapy and the lipodystrophy syndrome. Antivir. Ther. 6(1):9-20.

Joint United Nations Programme on HIV/AIDS (UNAIDS) (2013). Report on the Global AIDS Epidemic 2013. Available at: http://www.unaids.org/sites/default/files/media_asset/GARPR_2013_guidelines_en_0.pdf.

Kalyanasundaram AP, Jacob SM, Hemalatha R, Sivakumar MR (2012). Prevalence of Lipodystrophy and Dyslipidemia among Patients with HIV infection on generic ART in Rural South India. J. Int. Assoc. Physicians AIDS Care 11(5):329-34.

Matinez E, Domingo P, Galindo MJ, Milinkovic A, Arroyo J (2004). Risk of metabolic abnormalities in patients infected with HIV receiving antiretroviral therapy that contains lopinavir–ritonavir. Clin. Infect. Dis. 38(7):1017-23.

Mauss S, Wolf E, Jaeger H (1999). Impaired glucose tolerance in HIV-positive patients receiving and those not receiving protease inhibitors. Ann. Intern. Med. 130:162-163.

McLaughlin T, Abbasi F, Cheal K, Chu J, Lamendola C, Reaven G (2003). Use of metabolic markers to identify overweight individuals who are insulin resistant. Ann. Intern. Med. 139(10):802-9.

National Cholesterol Education Program (NCEP) (2002). The third report of the National cholesterol education program (NCEP) expert panel on detection, evaluation, and treatment of high blood cholesterol in adults (adult treatment panel III) final report. Circulation 106(25):3143-421.

Nery MW, Martelli CMT, Turchi MD (2011). Dyslipidemia in AIDS patients on highly active antiretroviral therapy. Braz. J. Infect. Dis. 15(2):151-55.

Pao V, Lee GA, Grunfeld C (2008). HIV therapy, metabolic syndrome, and cardiovascular risk. Curr. Atheroscler. Rep. 10(1):61-70.

Pefura Yone EW, Betyoumin AF, Kengne AP, Folefack FJK, Ngogang J (2011). First-line antiretroviral therapy and dyslipidemia in people

living with HIV-1 in Cameroon: a cross-sectional study. AIDS Res. Ther. 8:33.
Sharma B (2011). The antiHIV-1 drugs toxicity and management strategies. Neurobehav. HIV Med. 3:1-14.
Sharma B (2014). Oxidative stress in HIV patients receiving antiretroviral therapy. Curr. HIV Res. 12(6):13-21.
Sudano I, Spieker LE, Noll G, Corti R, Weber R, Lüscher TF(2006). Cardiovascular disease in HIV infection. Am. Heart J. 151(6):1147-55.
Tashima KT, Bausserman L, Alt EN, Aznar E, Flanigan TP(2003). Lipid changes in patients initiating efavirenz- and indinavir-based antiretroviral regimens. HIV Clin. Trials. 4(1):29-36.
The Data Collection on Adverse Events of Anti-HIV Drugs (DAD) Study Group (2003). Combination antiretroviral therapy and the risk of myocardial infarction. N. Engl. J. Med. 349(21):1993-2003.
Tomazic J, Silic A, Karner P, Vidmar L, Maticic M, Poljak M, Ihan A, Janez A (2004). Lipodystrophy and metabolic abnormalities in Slovenian HIV-infected patients. Wien Klin Wochenschr. 116 (21-22):755-9, 21.
Tungsiripat M, Aberg JA (2005). Dyslipidemia in HIV patients. Cleve. Clin. J. Med. 72(12):1113-1120.
Van der Valk M, Kastelein JJ, Murphy RL, Van Leth F, Katlama C, Horban A, Glesby M, Behrens G, Clotet B, Stellato RK, Molhuizen HO, Reiss P (2001). Atlantic Study Team: Nevirapine-containing antiretroviral therapy in HIV-1 infected patients results in an antiatherogenic lipid profile. AIDS 15(18):2407-14.
van Leth F, Phanuphak P, Stroes E, Gazzard B, Cahn P, Raffi F, Wood R, Bloch M, Katlama C, Kastelein JJ, Schechter M, Murphy RL, Horban A, Hall DB, Lange JM, Reiss P (2004). Nevirapine and efavirenz elicit different changes in lipid profiles in antiretroviral therapy-naïve patients infected with HIV-1. PLoS Med. 1(1):e19.
World Health Organization (WHO) (2010). Antiretroviral Therapy for HIV Infection in Adults and Adolescents. Recommendations for a Public Health Approach. Available at: http://whqlibdoc.who.int/publications/2010/9789241599764_eng.pdf
Young J, Weber R, Rickenbach M, Furrer H, Bernasconi E, Hirschel B, Tarr PE, Vernazza P, Battegay M, Bucher HC (2005). Lipid profiles for antiretroviral-naïve patients starting PI- and NNRTI-based therapy in the Swiss HIV cohort study. Antivir. Ther. 10(5):585-91.