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Research Article

THE EFFECTS OF DIFFERENT ANTIRETROVIRAL THERAPY COMBINATIONS UPON LIPID PROFILE OF HIV-POSITIVE PATIENTS IN LIBYA

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Abstract

Background: Using anti-retroviral therapy for HIV positive subjects has been reported to be linked to metabolic abnormalities such as altered serum lipid profile parameters. **Materials and Methods**: This study involved a hundred-one Libyan ART-treated HIV-1 subjects were on Different ART regimens and twenty-one untreated "Naïve" from Benghazi Medical Center and Benghazi center for infectious diseases and immunology during 2018-2019 and seventy age-matched HIV-negative subjects used as control. **Aim:** to assess total cholesterol (TC), triglycerides (TG), lipoproteins and other investigations such as viral load, CD4 and CD8. **Results;** TC, TG and LDL-C levels of HIV positive (122) subjects were highly significant (P <0.001) increased compared to HIV-negative subjects, whereas, HDL-C and LDL/HDL risk ratio were not significantly altered. TC, TG and LDL-C in the 4 ART-treated HIV subgroups were significantly (P <0.001) increased compared with ARV-Naïve and control groups. The CD4 count in the ARV treated-HIV subjects were significantly (P <0.014) lower compared CD4 count of untreated HIV group. **Conclusion:** The findings in the present study were in accordance with many other studies and suggests an association between HIV and dyslipidemia (specifically when protease inhibitor used) that is potentiated by receiving ART regimens. Monitoring lipid profile continuously become a necessity during the ART application.

Keywords: Antiretroviral Therapy, HIV.

INTRODUCTION

AIDS remains one of the most serious threats to public health in all parts of the world and it is considered as one of the 10 leading causes of death worldwide. HIV is classified as a member Retroviruses class and sub family Lentiviridae. The HIV causes the well-known known condition acquired immunodeficiency syndrome (AIDS) which is a life-threatening disease characterized by a great disruption of immune system. This condition showed a progressive infection of $CD4^+$ cells leading to immunosuppression that finally resulted in the symptoms and complications of AIDS (Deeks *et al.,* 2013). According to WHO reported that HIV caused about 40.1 million deaths (https://www.who.int/news-room/fact-sheets/detail/hiv-aids). The incidence continues to high, about 4000 people acquired HIV infection each day. If the current situation continues, 1.2. million individuals will acquire the infection by 2025. During the last two years, COVID and political crises have had a huge negative impact on individuals living with HIV and also affected WHO response to the HIV pandemic (UNAIDS Global AIDS Update 2022). Financially, the pandemic caused a great burden as it is predicted to cost about 109.8 billion US dollars in the coming 20 years (Schneider *et al.,* 2016). In Libya, a recent study in 2019, reported that the total number of individuals living with HIV infection was 8486 which is not high compared to other African countries (Daw *et al.,* 2019). The establishment of antiretroviral therapy (ARV) in 1990 lead to diminishing morbidity and mortality due to HIV infection and its related conditions (Palella *et al.,* 1998).

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According to WHO (ART Guidelines, 2013), the first-line of ART regimen includes using 2 nucleotide/nucleoside reverse transcriptase inhibitors "NRTIs" [lamivudine (3TC) and tenofovir (TDF)] with non-nucleotide/nucleoside reverse transcriptase inhibitor (NNRTI), for instance, nevirapine (NVP) and efavirenz (EFV). The second-line ARV regimen of protease inhibitor (PI) in combination with NRTIs. The use of ARV drugs causes a suppression of HIV-1 the replication which can be monitored by investigating the HIV load (viral load) and also by estimation of the $CD4^+$ cell count. Increases in the later is a sign of recovery of the immune system. Furthermore, ARV treatment significantly delayed the progression of the disease with obvious reduction in the incidence of opportunistic infections. The overall outcome of the use of ARV drugs was observed in the reduction morbidity and mortality rates and improvement of the quality of life that finally resulted in increased life expectancy of HIV patients (Lohse *et al.,* 2007). Despite the various benefits of ARV combinations, there are marked alterations in lipid profile in HIV and AIDS patients receiving ARV drugs as demonstrated in many recent evidences. The increased levels of blood lipids are considered as a risk factor for cardiovascular disease (CVD) (Carr *et al.,* 1998, Ridler *et al.,* 2003). Recent studies (Graham 2000, Fauvel *et al.,* 2001, Hruz *et al.,* 2001) suggested that using PI on the long may have atherogenic effects including increased serum triglyceride levels, increased levels of low-density lipoprotein (LDL-C), and reduced serum levels of high-density lipoprotein HDL-C. Furthermore; the changes on lipid metabolism were also confirmed by the work of Galli *et al.,* (2002) who reported alterations lipid metabolism in healthy adult after using ARVs including NRTIs, NNRTIs, and PIs. Based on the guidelines for the use of antiretroviral drugs, there are 6 classes of ART available for

the treatment of HIV including; PI, NRTIs, and NNRTIs, fusion inhibitor (FI), CCR5 antagonists and Integrase inhibitor that are currently used to treat HIV-1-infected individual belonging to different age groups (AIDS Info 2011). In treatment situations in which reverse transcriptase inhibitors-based regimens failed to treat HIV infected children, the next available option was the second line treatment of double boosted protease inhibitors (saquinavir, lopinavir, and ritonavir). Among these treatment classes; PI, NRTIs, and NNRTIs are the most frequently linked to the various alterations in lipid parameters in HIV-infected individuals (Zou and Berglund 2007, Mallewa *et al.,* 2009). Furthermore, metabolic changes in lipid metabolism in response to ART were dependent on the treatment regimen used. In the current study, HIV-1 patients were receiving three treatment regimens (each include triple combination therapy) of antiretroviral drugs. The aim of the present work is to investigate and compare the effects of different regimens of ARV treatments upon the lipid profile in Libyan HIV patients.

MATERIALS AND METHODS

Study design: Retrospective study was conducted in Benghazi center for infectious diseases and immunology (BCIDI) and Benghazi Medical center (BMC) to investigate lipid profile parameters and other biochemical tests in HIV patients under different antiretroviral drug regimens and HIV individuals who were not using ARV drugs (Naive) and comparing the results with healthy control group (composed of age-matched HIV negative individuals).

Blood sampling

2 types of blood samples were used in the present work, in the 1st type blood were collected into plain tubes to separate serum and in the 2nd, blood were collected in ethylene diaminetetra acetic acid "EDTA". The serum samples investigated in clinical chemistry analyzer Cobas Integra 400 plus for estimation of lipid profile. HIV viral load (HIV-1-RNA) was performed by real time PCR from Abbott. CD4 and CD8 counts were assessed using flow cytometry instrument (Facs calibuer). The viral load for HIV was investigated by real time PCR (Abbott; full automated machine). It is assessed by Abbott Real Time HIV-1 (m2000sp) assay uses RT-PCR to generate amplified product from the RNA genome of HIV-1 in clinical samples. Lymphocytes counts (CD4 and CD8) were assessed by the BD FACS Calibur (full automated instrument) depends on single platform technology which designed to perform absolute and percentage counts of both types of lymphocytes. Samples were prepared based on manufacturer instruction. The serum levels of Lipid profile parameters; total cholesterol (TC), HDL cholesterol, LDL cholesterol and triglycerides (TAG) were investigated by CHOD/PAP, PEG-precipitation, homogeneous enzymatic colorimetric assay and GPO/PAP methods respectively. The study results of lipid profile were interpreted using the traditional lipid profile panel (Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults, 2001-**Table 1**).

Statistical analysis

The data collected in data sheet were recorded in Microsoft Excel then imported in (Statistical Package for Social Sciences) SPSS version 26 and the statistical analysis. Values considered significant at $p<0.05$ at confidence interval 95%.

Table 1. Normal range and high ranges of Lipid profile

Parameter	Status description	Range
Total cholesterol	Desirable (low)	<200 mg/dl
	Borderline high	200-239 mg/dl
	High	240 mg/dl
Triglycerides	Desirable (low)	<150 mg/dl
	Borderline high	150-199 mg/dl
	High	200-499 mg/dl
	Very high	500 mg/dl
LDL- cholesterol	Desirable (low)	<100 mg/dl
	Acceptable	100-129 mg/dl
	Borderline high	130-159 mg/dl
	High	160-189 mg/dl
	Very high	190 mg/dl
HDL-cholesterol	Desirable (high)	> 60 mg/dl
	Acceptable	40-60 mg/dl
	Low	< 40 mg/dl

RESULTS

The total number of study population was 192 subjects, the percentage of males was 47.52% whereas percentage of females was 52.48%. The HIV-positive patients using ART regimens were distributed into 4 groups as showed in Table 2 (in material methods section) and the percentage of each group was shown in Figure 1.

Table 2. HIV positive cases classified based on treatment regimens

	ART groups	Drug combinations	No. of HIV cases
G1	2NRTIs +NNRTI	FTC + TDF + EFV	36
G2	2NRTIs+ PI	FTC+ TDF + LPV/r	25
G3	2NRTIs +INSTI	FTC+ TAF + EVG/c	22
G4	2NRTIs +INSTI	FTC+ TDF + RAL	18

Where; **G1** includes: **2NRTIs** include: Emtricitabine (FTC) and Tenofovir (TDF); **NNRTI** is Efavirenz (EFV); **G2**: includes the same **2NRTIs** plus **PI** is Lopinavir (LPV); **G3**: includes **2NRTIs** and **INSTI** (Integrase Strand Transfer Inhibitor) include Elvitegravir (EVG) whereas; **G4** is similar to G3 and include Raltegravir (RAL) as Integrase inhibitor.

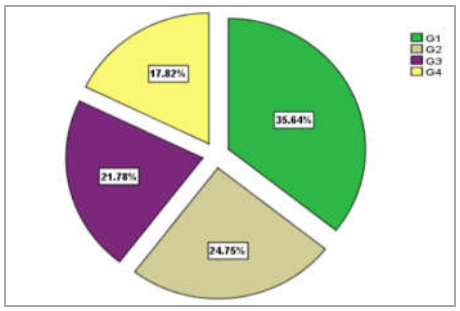

Figure 1. The percentage of ART-treated HIV subjects distributed into 4 subgroups Depending on treatment combinations

Comparing HIV viral load among ARV-treated HIV subgroups and untreated HIV (ARVs Naïve)

Viral load among HIV positive subjects showed no significant ($P > 0.05$) differences among different ARV-treated HIV subgroups and untreated HIV (ARVs Naïve).

Evaluation of viral load among HIV positive subjects

The distribution of HIV positive subjects according to their viral load showed that most cases 82 (67.2%) in this study had undetectable viral load (<1000 copies/ml), 35 cases (28.7%) showed detectable low viral load (1000-100000 copies/ml), 4 cases only (3.3%) recorded detectable high viral load (100000-

1000000 copies/ml) and 1 case (0.8%) with extremely high viral load (>1000000 copies/ml) as shown in **Figure 2**.

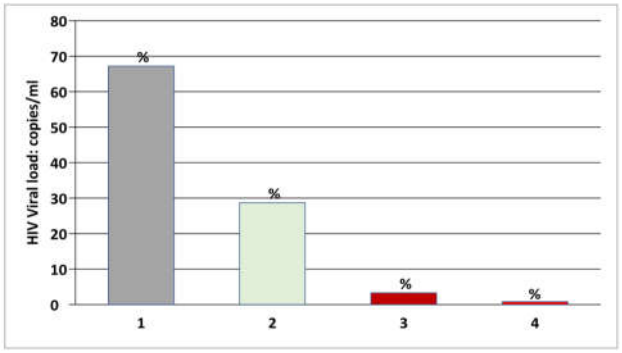

Figure 2. Distribution of HIV positive subjects according to their viral load

Comparing $CD4^+$ and $CD8^+$ counts in HIV positive subgroups

By comparing the means of $CD4^+$ and $CD8^+$ counts among ARV-treated HIV subjects with different ARV treatments (G1, G2, G3, G4) and ARVs Naïve group, a significant difference in the means of $CD4^+$ counts were found (P <0.05), higher $CD4^+$ counts were detected in subgroups G2 and G1. Whereas no significant differences in the mean of $CD8^+$ counts among these groups were found (P >0.05), as represented in Table 3 and Figure 3.

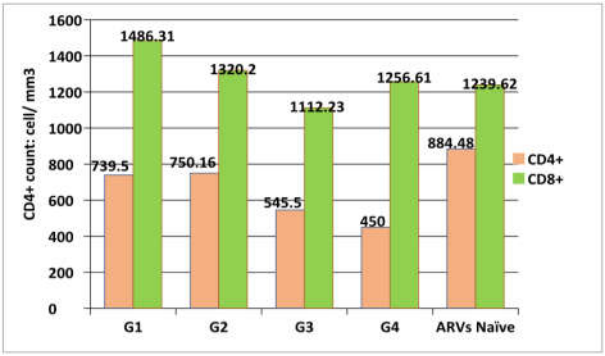

Figure 3. Comparing $CD4^+$ and $CD8^+$ counts among HIV positive subgroups and untreated-HIV (ARVs Naïve) group

Comparison of lipid profile parameters between HIV positive cases and control

Cholesterol, triglycerides and LDL-C levels of HIV positive (122 subjects) were highly significant (P <0.001) increased compared to HIV-negative subjects (70 subjects) as shown in **Table 3**. On the other hand, HDL-C levels and LDL/HDL risk ratio values of were statistically not significant (P > 0.05) between both of the study groups.

Table 3. Comparison of lipid profile between all HIV positive cases and control

Parameters	Study Groups	N	Mean	P value
Cholesterol	Total HIV positive	122	169.89	P < 0.001
	Control	70	151.16	
Triglycerides	Total HIV positive	122	139.44	P < 0.001
	Control	65	79.28	
LDL-C	Total HIV positive	122	114.28	P < 0.0001
	Control	70	93.04	
HDL-C	Total HIV positive	122	48.09	P > 0.05
	Control	70	46.96	
LDL/HDL	Total HIV positive	122	2.716± 1.254	(P > 0.05)
	Control	70	2.331± 1.512	

Cholesterol levels among study population

ART-treated HIV cases showed the highest levels of cholesterol with 9 high cholesterol cases (8,9%) and 11cases (10.9%) with borderline high cholesterol the rest 81 cases (80.2%) showed normal levels, whereas the whole 21 cases (100%) untreated-HIV cases showed normal cholesterol levels (Table 4).

Table 4. Distribution of study subjects according to cholesterol levels

Cholesterol	ARV-treated HIV		ARVs Naïve	
	N.	Percent	N.	Percent
Normal	81	80.2	21	100.0
Border line	11	10.9	-	-
High	9	8.9	-	-

Cholesterol levels among ART-HIV subgroups

The subgroup G2 (2NRTIs + PI) showed a high percentage of elevated serum cholesterol 6 (24%) cases and borderline cholesterol levels 5 (20%), the remaining cases showed normal samples, compared to G1 (2NRTIs + NNRTI) which included 3 cases (8.3%) high and 2 (5.6%) borderline levels. In G3 and G4 subgroups (2NRTIs + INSTI), borderline cholesterol was 3 (13.6%) and 1 (5.6%) respectively and the remaining samples were normal **(Figure 4)**.

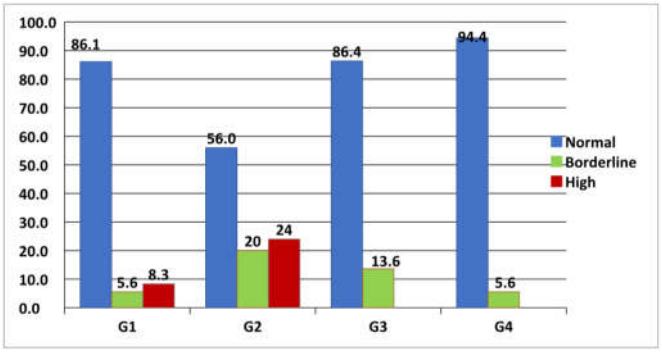

Figure 4. Cholesterol levels among ARV treated-HIV subgroups

Comparing cholesterol level among ARV-HIV subgroups and other groups

There were significant (P <0.001) increase in serum cholesterol of G2 subgroup compared with other subgroups as well as the control and ARV-Naïve groups. The later 2 groups showed the least cholesterol levels as shown in **Figure 5**.

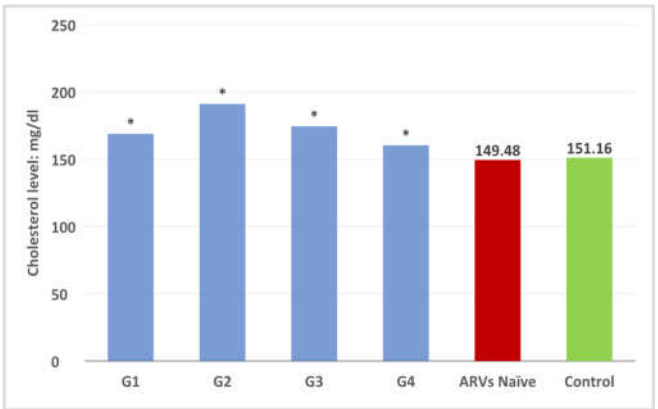

Figure 5. Comparing cholesterol level among all subgroups

Distribution of study subjects according to their triglyceride levels (TG)

By comparing the three main groups, we found that almost of high and borderline high TG cases were found in ARV-treated HIV group; 22 cases (21.8%) and 16 cases (15.8%), respectively whereas only 1 (1%) subject showed very high TG levels compared with only 2 high TG cases in untreated HIV as shown in Table 5.

Table 5. Distribution of study subjects according to their triglyceride levels

Triglyceride	ARVs treated HIV		Untreated HIV	
	N.	Percent	N.	Percent
Normal	62	61.4	18	85.7
Borderline High	16	15.8	1	4.8
High	22	21.8	2	9.5
Very high	1	1.0	-	-

Distribution of HIV-treated subgroups according to triglyceride levels

The distribution HIV positive subjects on ARVs according to their triglyceride levels showed that, the subgroup G1 showed 27 (75%) showed normal, 1 (2.8%) borderline and 8 (22.8%) high triglyceride levels, the second subgroup G2 showed 11 (44%) normal triglyceride levels, 4 (16%) borderline, 10 (40%) high triglycerides levels, the third subgroup G3 showed 10 (45.5%) normal, 8 (36.4%) borderline, 3 (13.6%) high and 1 (4.5%) very high triglyceride levels, the fourth subgroup G4 showed 14 (77.8%) normal, 3 (16.7%) borderline and 1 (13.6%) high triglyceride levels as represented in the table (3-11) and Figure 6.

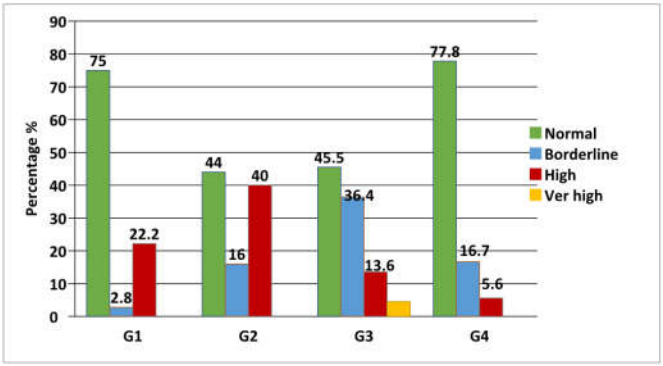

Figure 6. Distribution of HIV-treated subgroups according to triglyceride levels

Comparing triglyceride levels among all study subgroups

By comparing triglyceride levels among the study subgroups, significant differences in the means of triglycerides levels were noticed ($p < 0.001$). Higher triglycerides level was recorded in the subgroup G3 followed by G2, comparable triglyceride levels were detected in subgroups G1 and G4, while ARVs-Naïve and control reported least triglyceride levels **(Figure 7).**

Distribution of study subjects according to their LDL levels

ARV-treated HIV subjects showed 28 (27.7%) normal, 46 (45.5%) acceptable, 11 (10.9%) borderline, 13 (12.9%) high and 3 (3%) very high LDL levels. HIV positive Naïve subjects showed 10 (47.6%) normal, 7 (33.3%) acceptable and 4 (19%) borderline LDL levels (**Table 7)**.

Table 7. Distribution of study subjects according to their LDL levels

LDL	ARV-treated HIV		ARV Naïve	
	N.	Percent	N.	Percent
Normal	28	27.7	10	47.6
Acceptable	46	45.5	7	33.3
Borderline high	11	10.9	4	19.0
High	13	12.9	-	-
Very high	3	3.0	-	-

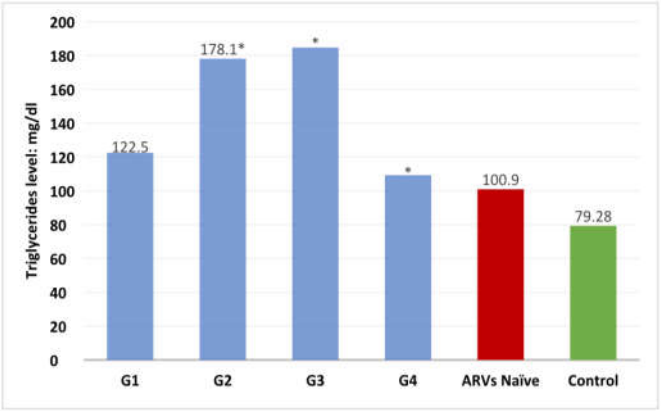

Figure 7. Comparing triglyceride levels among HIV positive and control subjects

Distribution of ARV-treated HIV subgroups according to LDL levels

In the subgroup G1 12cases (33.3%) normal, 19 (52.8%) acceptable, 2 (5.6%) borderline, 2 (5.6%) high and 1 (2.8%) very high LDL level. In the second subgroup G2 6 cases (24%) normal, 8 (32%) acceptable, 2 (8%) borderline, 7 (28%) high and 2 (8%) very high LDL levels. In the third subgroup G3 showed 6 cases (27.3%) normal, 7(31.8%) acceptable, 7 (31.8%) borderline, 2 (9.1%) high LDL levels. In the fourth subgroup G4 4 cases (22.2%) normal, 12 (66.7%) acceptable and 2 (11.1%) high LDL levels, higher percentage of high and very high LDL levels were recorded in the second subgroup G2 as represented in (Figure 8).

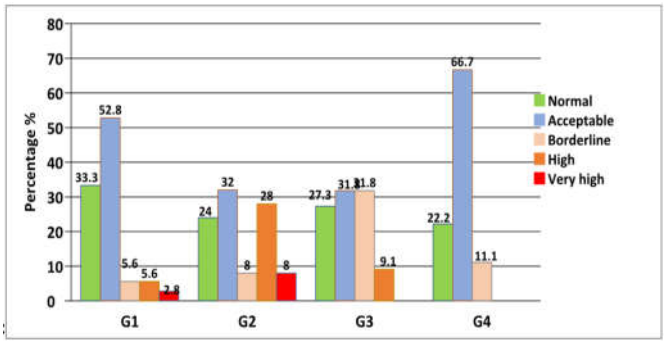

Figure 8. Distribution of ARV-treated HIV subgroups according LDL levels

Comparing serum LDL of ARV-treated HIV subgroups with study groups

By comparing serum LDL levels among the study subgroups, significant differences in the means of serum LDL levels were noticed ($p < 0.001$). Higher serum LDL level was recorded in the subgroup G2 followed by G3, comparable serum LDL levels were detected in subgroups G1 and G4, while ARVs-Naïve and control reported least serum LDL levels (Figure 9).

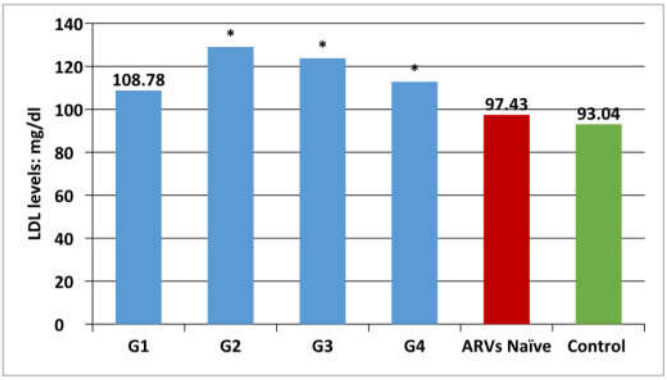

Figure 9. Comparing serum LDL of ARV-treated HIV subgroups with other study groups

Evaluation of HDL Levels

Distribution of study subjects according to their HDL

HIV positive subjects on ARVs group showed 22 cases (21.8%) normal, 48 (47.5%) acceptable, 31 (30.7%) low HDL levels. while ARVs Naïve subjects showed 5 cases (23.8%) normal, 7 (33.3%) acceptable and 9 (42.9%) low HDL levels, Table 8.

Table 8. Distribution of study subjects according to their HDL levels

HDL	HIV positive on ARVs		ARVs Naïve	
	N.	Percent	N.	Percent
Normal	22	21.8	5	23.8
Acceptable	48	47.5	7	33.3
Low	31	30.7	9	42.9

Distribution of study subgroups according to their HDL levels

The subgroup G1 showed 20 cases (22%) normal, 39 (42.8%) acceptable, 32 (35.2%) low HDL levels. The second subgroup G2 showed 8 cases (22.2%) normal, 19 (52.8%) acceptable, 9 (25%) low HDL levels. The third subgroup G3 showed 6 cases (24%) normal, 13(52%) acceptable, 6 (24%) low HDL levels. The fourth subgroup G4 showed 5 cases (27.8%) normal, 4 (22.2%) acceptable and 2 (11.1%) high triglyceride levels, higher percentage of high and very high LDL levels were recorded in the second subgroup G2. Distribution of study subgroups according to their HDL levels is represented in Figure 10.

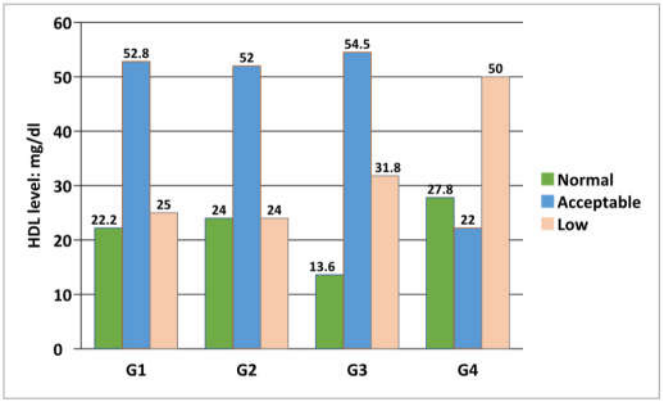

Figure 10. Distribution of study subgroups according to their HDL levels

Comparing HDL levels among all study subgroups

By comparing all study subgroups, no significant (p- > 0.05) differences were found in the means of HDL levels between these subgroups as shown in Figure 11.

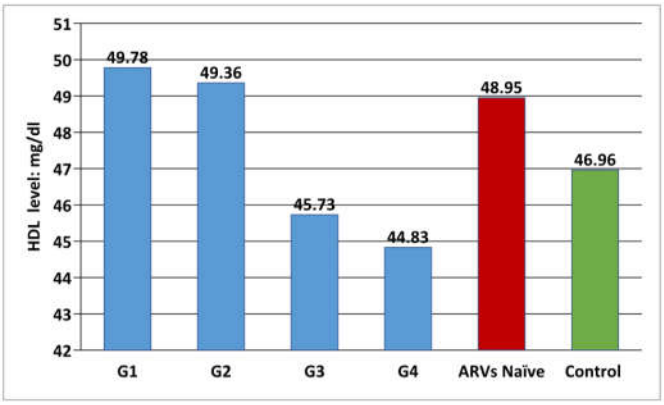

Figure 11. Comparing HDL levels in HIV positive subgroups on ARVs.

Comparing LDL/HDL ratios among the study subgroups

The mean values of LDL/HDL ratio were statistically not significant (P >0.05) among the four study subgroups, ART-naïve group and healthy control group as shown in the Figure 12.

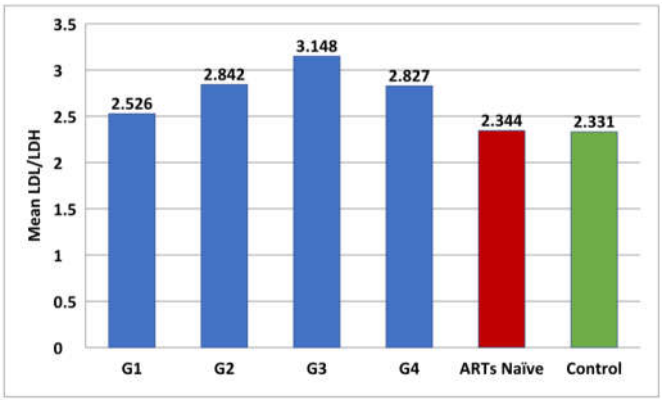

Figure 12. Comparing LDL/HDL values in HIV positive subgroups on ARTs

DISCUSSION

Recently, WHO recommended combining two NRTI with one of NNRTI [3]. This drug combination is comparable to the one used in group1 (FTC + TDF + EFV) which represents a first line treatment for HIV infection. Our second HIV-treated group 2 included a PI (Lopinavir/r) which become an obligatory drug of 2nd line treatment regimen following unsuccessful applications of the 1st line regimen (Tadewos *et al.,* 2012, United Nations Joint Programme on HIV/AIDS (UNAIDS). Group 3 and 4 treatment regimen include new drugs called integrase inhibitor [Elvitegravir (EVG) and Raltegravir (RAL), respectively. The application of ART regimens in our study resulted the control of HIV infection among HIV positive cases. This was revealed by viral load values which showed that most of the HIV positive cases (82 cases, 67.2%) in this study had undetectable viral load (<1000 copies/ml) and only about 4% of the cases showed higher viral

load (>100,000 copies/ml). These finding indicated a high degree of effectiveness of the ART treatment and a good prognosis for our HIV patients. Our findings were in agreement with a report of UNAIDS, 2010, which showed that among all people living with HIV 77% had suppressed viremia [4]. These results were in the same line with recent population-based study (2020) in the African country Zimbabwe (Ministry of Health and Child Care, MoHCC). In the current work, the mean $CD4^+$ counts among ART-treated HIV were 648 Cells/mm^3 which was significantly lower than ART naive HIV subjects (884 Cells/mm^3). These was results were not in accordance with a recent work in Ethiopia (Tilahun *et al.,* 2022), in which the mean CD4 cell Count (500 Cells/mm^3) on ART treated group was significantly higher than ART naive HIV subjects (339 Cells/mm^3). However, CD4 cell count was not significantly associated with dyslipidemia and lipid profile level. This might be due to HAART effect on improving immunological status of HIV subjects. In the same line, $CD4^+$ and $CD8^+$ counts among ARV-treated HIV subjects with different ARV treatments, the means of $CD4^+$ counts were lower ($P < 0.003$) in subgroups G2 and G1than that of ARVs Naïve group, but they were higher compared to G3 and G4 subgroups. These findings indicated that these 2 ART regimens succeeded in controlling the state of inflammation reflected by the rise in CD4 counts. Monitoring CD4 count represents a marker of status of the immune system, patient response to treatment and also gives valuable guidance for doctors regarding using ART for HIV-positive subjects (Bouteloup *et al.,* 2017). Cholesterol, triglycerides and LDL-C levels of HIV positive (122 subjects) were highly significant ($P < 0.001$) increased compared to HIV-negative subjects (70 subjects). On the other hand, HDL-C levels and LDL/HDL risk ratio values of were statistically not significant ($P > 0.05$) between both of the study groups. All the parameters of lipid profile of HIV positive subjects (TC, LDL-C, HDL-C, TG and LDL/HDL-C ratio) in the current study, were significantly higher compared to HIV-negative subjects (control), which indicate an effect of the HIV infection potentiated by the use of ART upon metabolic state of those patients. Furthermore, ART-treated HIV subjects showed 8.9% high cholesterol cases out of 101 cases whereas no high cholesterol found among ARVs Naïve group and control. These finding are in agreement with Tilahun *et al.,* 2022.

In previous research, the use of ART regimen containing two NRTI + one PI (or 2 PI) resulted in hypercholesterolemia (Jones *et al.,* 2005, Pupulin *et al.,* 2008). Similar results were reported in the current study, in which the subgroup G2 (2NRTIs + PI) showed a high percentage of elevated serum cholesterol 6 (24%) cases and borderline cholesterol levels 5 (20%) compared with the other subgroups (G1, G3 and G4) that included different ART regimen. The prevalence of hypertriglyceridemia in the present study among ART treated subjects were 22% compared with 9.5% in ARTs naïve group. This finding is much lower than the percentage of high TG levels (59.6%) in ART treated reported in Ethiopia and in Kano, North-Western Nigeria (43.3%) Mohammed, I.A. Yahaya 2015. In a similar manner to cholesterol prevalence, G2 subgroup (includes PI) showed the highest percentage of raised TG (40%) and very high TG (4.5%). This finding is lower than the prevalence of hypertriglyceridemia (52%, triglycerides more than 250 mg/dL) reported by Vergis et al. (2001) in which ART included PI. Higher levels of TG in HIV appeared at the beginning of the infection. Interferon-alpha may cause elevated TG via two mechanisms: firstly, through a reduction in clearance of TG and secondly via enhancing hepatic synthesis citrate (Grunfeld *et al.,* 1992). Furthermore, Subgroup G4 (using raltegravir RAL) showed the most favourable lipid profile with 77.8% normal triglycerides. This finding is in agreement with Saumoy *et al.,* 2021who reported that RAL and Elvitegravir (EVG/c) have a better lipid profile compared with NNRTI and boosted PI. In switching studies, Both RAL and EVG/c are characterized by significant reduction in serum lipoproteins. On the other hand, Both G2 (using PI; LPV/r) and G3 (using integrase inhibitor; EVG/c) showed significantly higher means of serum TG (178, 184.7 respectively) compared to other ART-treated subgroups, ARTs naïve group and control. In support of the highest level of TG in G3, the prevalence of abnormally high transaminases (ALT and AST) was 9.5% in G3, indicating that this treatment combination has a high degree of toxicity compared to other subgroups. whereas G4 showed the least serum TG levels (mean: 109 mg/dl). The normal TG levels in this group were supported by the lowest levels of serum ALT: 16 U/l and AST: 19 U/l reported in our study which were very close to the control levels.

In the present work, the prevalence of high and very high levels of LDL-C was 12.9% and 3%, respectively, of the ART-treated HIV group whereas, no high LDL-C cases reported in the ARV-HIV positive Naïve subjects. These results were lower than the findings of Tao, *et al.,* 2009 who found a prevalence of 17.5% hypercholesterolemia in HIV patients receiving ART. Furthermore, the highest prevalence of high and very high LDL levels was reported in subgroup2 (using PI) were 28% and 8% respectively, which is consistent with the significantly ($P < 0.001$) higher LDL-C in G2 (receiving PI) compared with untreated HIV and control. In addition, There was a negative correlation between CD4 and LDL-C (r = -0.515, p-value <0.05), LDL reduced with increased $CD4^+$ counts. Our finding is lower than the work of Fauvel *et al.,* 2001 and Panse *et al.,* 2000 who reported increased serum lipid abnormalities above 70% of HIV subjects receiving protease inhibitors included in ART combination. On the other hand, our findings were higher than Pupulin et al. 2008 who find 3% of high LDL-C in HIV patients using PI as a component of ART regimen. The percentage of Low HDL levels among HIV positive subjects on ARTs showed 22 was 31subjects (30.7%). This finding is lower than that of Tilahun *et al.,* 2022 and Bernal *et al.,* 2008, who found Low HDL prevalence of 50% and 45, respectively. On the other hand, the previous finding is the same as the prevalence of low HDL (50%) in subgroup 4 (2NRTIs+RAL). On the other hand, the HDL levels in HIV treated subgroups were non significantly altered compared with untreated HIV and healthy control which is on the contrary with the previous evidence. In on ART-treated HIV subjects there was significant correlations (r= 0.237, p-value <0.05) between $CD4^+$ and HDL levels (HDL increased with increased $CD4^+$ counts), LDL/HDL ratio used as an indicator of the degree of atherogenicity, in the present work, this ratio was not significantly altered among the 4 study subgroups, compared to ART-naïve group and healthy control group which indicate a low risk of atherosclerosis and CVD. On the contrary, Nguemaïm *et al.,* (2010), found a significant ($p < 0.001$) increase in TC/HDL ratio of ART-treated HIV compared to HIV negative subjects. The ART combination containing protease inhibitors had the greatest impact upon lipid profile of HIV treated subjects in our study. The mechanism by which PI affect lipid indices involves inhibiting lipogenesis and to trigger lipolysis of fat. NRTIs which is used

along with PI, diminishes lipogenesis and adipocyte differentiation in fat tissue, collectively these effects were suggested to be a cause of mitochondrial toxicity, and may also lead to inhibition of the action of γ- DNA polymerase in the mitochondria, that finally reduce the amount of mitochondrial DNA (Grinspoon and Carr, 2005, Christeff *et al.,* 2002).

Conclusion

The findings in the present study were in accordance with many other studies in different countries and suggests an association between HIV and dyslipidemia that is potentiated by receiving ART regimens. As it is well known dyslipidemia is considered as one of the risk factors for CVD. It is important to monitor lipid profile continuously during the application ART (especially that contains PI) in HIV positive subjects to avoid the serious complications caused by dyslipidemia.

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