European Journal of Molecular & Clinical Medicine
ISSN 2515-8260 Volume 07, Issue 08, 2020

The Effect Of Highly Active Antiretroviral Therapyon Lipid Profileof Hiv Patients

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Abstract: Background:The widespread use of highly active retroviral therapy (HAART) has indicated a dramatic reduction in impairment due to immunodeficiency. Several studies have shown that an adverse event of HAART on dyslipidemia and insulin resistance. This study aimed to assess changes in lipid profiles after HAART.

Methods:A prospective cohort study with a consecutive sampling method consists of 59 HIV-infected patientsreceiving HAART at Dr. Wahidin Sudirohusodo Hospital, Makassar, Indonesia, from March-September 2020. Lipid profiles were measured at the initial time and after three months of HAART. The drug regimen was divided into two groups: Regimen

group 1 (tenofovir, lamivudine, efavirenz), and another regimen group (consist of 4 regimen group combination: zidovudine, lamivudine, efavirenz; tenofovir, emtricitabine, lopinavir/ritonavir; tenofovir, lamivudine, nevirapine, and tenofovir, lamivudine, rilpivirine). ANOVA paired t-test and chi-square test were used for statistical analysis(it is significant if p is<0.05).

Results:The mean age of the subjects was 32.1 ± 6.6 years old. About 76.3% of subjects were male. Regimen 1 was used by 88.1% of the subjects and another regimen only 11.9% of the subjects. There were 27 subjects (45.8%) were underweight. The proportion of subjects with lipid abnormalities after 3 months of HAART significantly higher in LDL-c and TG level (P= 0.002 and 0.021). Regimen group1 showed increased levels of total cholesterol (TC), LDL-c, and TG (P = 0.037, 0.041, and 0.001) after HAART.

Conclusion:Highly active retroviral therapy is associated with lipid profile changes in HIV patients after 3 months of therapy.

Keywords: Human Immunodeficiency Virus, Lipid Profile, highly active antiretroviral therapy, Dyslipidemia

1. INTRODUCTION

Globally, 35 million people living with HIV, and 19 million do not know their HIV positive status. Indonesia is the 5th country most at risk of HIV/AIDS in Asia.(1) In 2018, the Directorate General of Disease Prevention and Management of the Indonesian Ministry of Health reported 114,065 HIV cases, 67.2% of the patients were men and 32.8% of them were women.(2) HAART was introduced and widespread in the mid-1990s and contributes to metabolic disorders, including dyslipidemia. Dyslipidemia is a potential atherogenic and may increase cardiovascular risk.(3)(4)(5) Patients with AIDS also have low HDL-c and LDL-c levels and a decrease in TG secretion.(6) Characteristics of dyslipidemia in HIV-infected patients receiving HAART are the increase of TC levels, LDL-c, and TG, and low levels of HDL-c.(7)

Highly active retroviral therapy is classified according to its mechanism of action and divided into five groups: Nucleoside reverse transcriptase inhibitors (NRTI), Non-nucleoside reverse transcriptase inhibitors (NNRTI), Protease inhibitors (PI), Integrase inhibitors (INSTI), CCR antagonists.(8)(9)(10)In PI-based therapy, HDL-c levels tend not to increase, and hypertriglyceridemia has been shown to get worse. In contrast, giving an NNRTI-based HAART regimen showed an increase in HDL-c about 40% depending on the agent used, with

increases in TC, LDL-c, and TG. The increase in TG is usually not as severe as that found in the PI regimen.[7]

This study aimed to assess changes in lipid profiles after HAART.

2. METHODS

This was a prospective cohort study at Dr. WahidinSudirohusodoHospital, Makassar, Sulawesi Selatan,Indonesia.A total of 59 new HIV-infected patients over 18 years old starting HAART were recruited by consecutive sampling from March to September 2020. The subjects who met the inclusion criteria and were willing to participate in signed informed consent (were included). Demographic data for all subjects were recorded, including age, sex, and body mass index (BMI). For laboratory evaluation, lipid profiles were examined before and after three months ofHAART. The HAART regimen was divided into two groups: regimen group 1 (tenofovir, lamivudine, efavirenz), and another regimen (consist of 4 regimen group combination: zidovudine, lamivudine, efavirenz; tenofovir, emtricitabine, lopinavir/ritonavir; tenofovir, lamivudine, nevirapine, and tenofovir, lamivudine, rilpivirine). Statistical analysis was performed using SPSS Version 22. Statistical analysis was performed using descriptive statistical calculations and frequency distribution, as well as ANOVA statistical tests, paired t-test, and chi-square test. The result is significant if p is <0.05. This study protocol was approved by the Health Research Ethics Commission, Medical Faculty, Universitas Hasanuddin with the approval letter number of 1208 / UN4.6.4.5.31 / PP36 / 2019.

3. RESULTS

Subject Characteristics

A total of 59 subjects were included in this study, with 45 males (76.3%) and 14 females (23.7%). The subjects' age was between 20-42 years old with a mean of 32.1 ± 6.6 years. Based on the body mass index (BMI), 27 (45.8%) subjects were underweight. Regimen 1 was the most widely used in this study, 52 subjects (88.1%), while another regimen was only used by 7 subjects (11.9%).

We found an increase in all lipid profile after 3 months of HAART. (Figure 1)

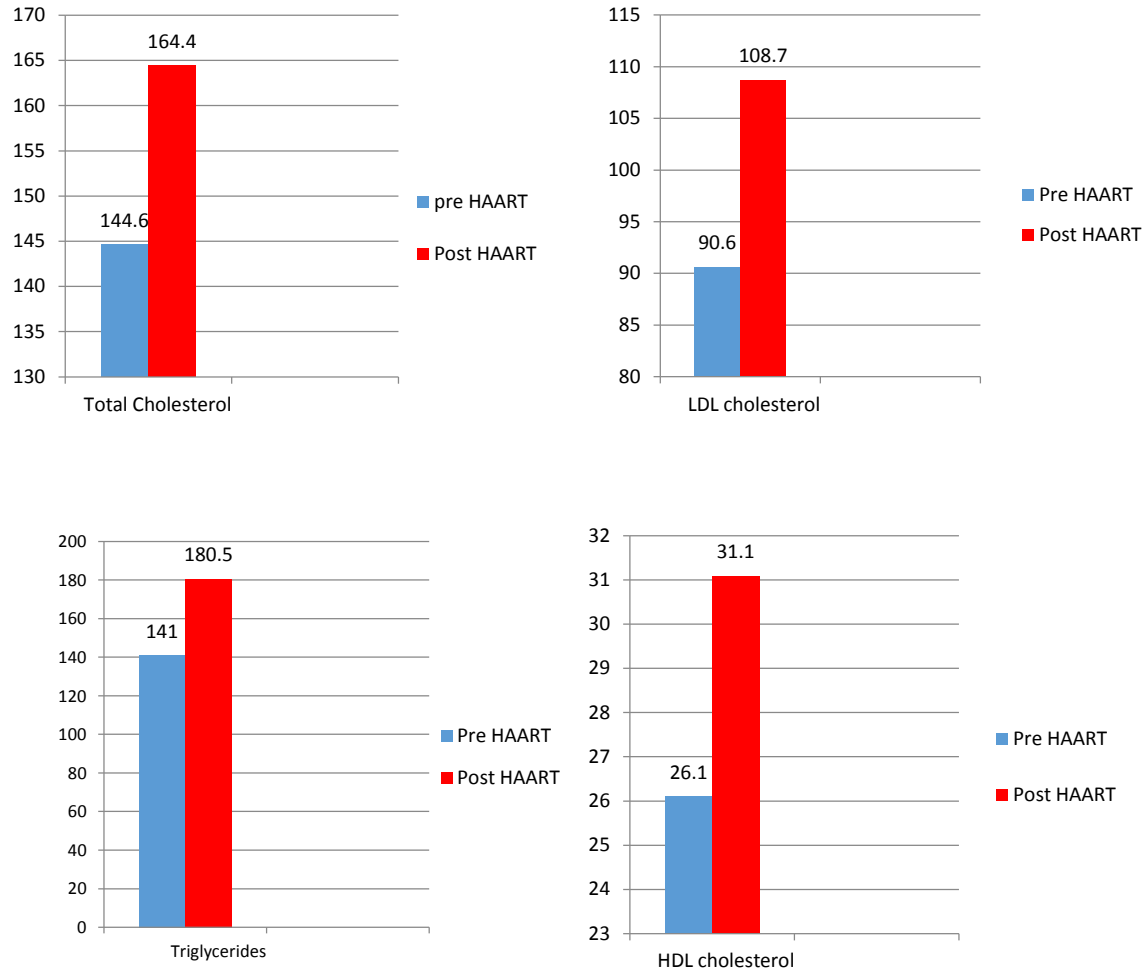

Figure 1. Alteration of lipid profile after 3months of HAART

Analysis of subjects proportion based on change of abnormalities of lipid fraction

Proportion of subject with lipid abnormalities after 3 months of HAART found significantly higher in LDL-c and TG level (P= 0.002 and 0.021). (Table 1)

Table 1. Subject proportion of lipid profile abnormalities before and after HAART (n = 59)

Variable	Pre HAART (n)	Post HAART (n)	*P**
Total cholesterol			
Normal	50	44	0.146
High	9	15	
LDL-c			
Normal	49	36	0,002
High	10	23	
Trigliserida			

Normal	51	41	0,021
High	8	18	
HDL-c			
Normal	0	4	NA
Low	59	55	

Chi-square test, NA : not available

Analysis of the changes in mean of lipid profiles according to HAART to regimen group 1

On the administration of regimen 1, there was a significant change in TC, LDL-c, and TG levels with significance levels respectively (P = 0.037; 0.041 and 0.001), while for HDL-c levels there was no significant change (P = 0.241). Because the other regimen group had only 1-2 subjects each, we only carried out the further analysis in the regimen group 1. (Table 2)

Table 2. Mean Levels of Lipid Profiles according to Regimen Group 1 HAART

REGIMEN	LIPID PROFILE	MEAN± SD	VALUE	*P**
Regimen group 1 (n = 52)	Total cholesterol pre HAART	145,4 ± 53,2		
	Total cholesterol post HAART	158,4 ± 55,7	+13,0	0,037
	HDL-c pre HAART	26,8 ± 13,9	+2,6	0,241
	HDL-c post HAART	29,4 ± 16,2		
	LDL-c pre HAART	89,8 ± 42,7		
	LDL-c post HAART	104,1 ± 53,2	+14,3	0,041
	Triglycerides pre HAART	141,8 ± 51,8		
	Triglycerides post HAART	182,2 ± 85,8	+40,4	0,001

**Independent t-test*

4. DISCUSSION

The current analysis included a total of 59 HIV-infected subjects, with a mean age of 32,1 ± 6,6 years.This case is in line with a study conducted by Pudjiati S et al. which reported that the highest number of HIV infections was found in the 20-29 years age group (38.69%).[11] It is considered that the age group is sexually active.

Most of the subjects were males (76.3%). This result is following by the national data fromThe Directorate General of Disease Prevention and Management in 2018 and The Joint United Nations Program on HIV and AIDS (UNAIDS), the prevalence of HIV infection is more among men, especially those who are homosexual, which increases in nearly 80 states.[2][12]

Most of the subjects were underweight (45.8%).This result is consistent with a study conducted by Malvy D et al.that reported more than 10% of the HIV-infected patients indicated of more weight loss, and this result can be used as a predictor of HIV disease progression in adults. Malnutrition is a phenomenon that often occurs during the HIV infection and is a major cause of morbidity. The causative factors are still not fully understood, which consist of decreased appetite, malabsorption of nutrients, metabolic disorders, and endocrine system dysfunction.[13]

Regimen group 1 is the highest proportion (88.1%) in this study, consisting of a combination of group 2 NRTI and 1 NNRTI, is the first choice of HAART based on the National Guidelines for HIV Management Medical Services 2019.[14] Also, another regimen consisted of a combination of NRTI and NNRTI groups as well as a combination of NRTI and PI. This data is in line with a study by Nery MW et al. that reported the highest use was by the combination of 2 NRTI and 1 NRTI followed by a combination of NRTI and PI.[15]

This study shows an increase in the mean lipid fractions before and after 3 months of HAART. This data consistent with the study by Ceccato et al. that reported a comparison of lipid profile levels before and after HAART showed an increase in all lipid profile levels.[16]

We noted a significant change in levels of LDL-c and TG were significantly found higher than those of the normal group. This result is in line with a study by Ji Shujing et al. reported that after HAART, TG levels significantly increased in the high TG group than in the normal group.[17] In another study, Singh J et al. reported that after 3-6 months of HAART, there is an increase in LDL-c.[18]

In our study, regimen group 1 showed a significant increase in mean TC, LDL-c, and TG levels after 3 months of HAART. According to a study conducted by Nsagha DS et al. reported that the mean of TC and TG values were higher in patients using tenofovir than zidovudine (NRTI), as well as using efavirenz versus nevirapine (NNRTI) could increase TC and TG levels.[19]

Another study by Van LF et al. reported that use of efavirenz caused a 49% increase in LDL-c compared to nevirapine only increased by 20%.[20]

This participant of this study only 59 subjects with 3 months observation. Thus, only regimens group 1 could be analyzed due to the lack of subjects in another regimen. Also, another factor that might affect the lipid profile is not controlled in this study. Those are the limitations of this study.

5. CONCLUSION

In conclusion, a regimen of HAART is associated with a change of lipid profile after 3 months of therapy.

6. REFERENCES

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