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Lipid Profile in HIV Infected Children Receiving Antiretroviral Treatment

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Abstract:

This study reviewed the lipid profile of human immunodeficiency virus/acquired immunodeficiency syndrome (HIV/AIDS) patients in relation to use of antiretroviral therapy (ART). Lipid profile is becoming one of the common problems in human immunodeficiency virus infected patients receiving antiretroviral therapy. Data on lipid profile derangements induced by antiretroviral treatment. The aim of this study was to assess the lipid profile abnormalities in HIV infected children receiving ART. ***Material and Method*** *- Information on sex, age, specific ART type in use , ART start date, duration of treatment, duration of HIV infection, BMI, relevant signs and symptoms and medications if any were collected by trained nurses using structured questionnaires and patients medical record.* ***Blood Sample Collection, Transport and Processing*** *- Following a standard and safety collection procedure, about 5 ml fasting venous blood was taken from the patients and the control groups by clinical nurses and senior laboratory technologist. Fasting serum samples were analyzed for total cholesterol (TC), triglyceride (TG), High Density Lipoprotein- Cholesterol (HDL-c). Low density lipoprotein cholesterol (LDL) and Very low density lipoprotein (VLDL) was determined by Friedewald Equation (13).* ***Result and conclusion*** *- There was statistically significant difference between the two groups for TC, TG, TC/HDL-c ratio and TG/HDL –c ratio. On the basis of our study we concluded that the level of TG, TC, HDL-c and VLDL-c is high in HIV positive populations receiving first line ART (group I) as compared to ART naïve (group II). Considering that these altered lipid profiles can be an independent risk factors for coronary artery diseases and myocardial infarction, treatment with first-line ART may actually have potential risks for cardiovascular health of HIV positive people receiving ART.*

Keywords *- ART, HIV, TC, TG, LDL-c, HDL-c, VLDL-c, AIDS and CD4*

Introduction

All HIV-infected children reach a point in their disease when they need antiretroviral treatment. Good nutritional care and support remains important if the child is to benefit optimally from ART. Most antiretroviral drugs do not need specific recommendations in relation to meals/foods, while some should not be taken with meals or with specific foods e.g. saquinavir and garlic. Although some antiretroviral drugs can lead to late complications such as anaemia, lipodystrophy, and diabetes these can generally be managed and ART continued. Overall the benefits of ART far outweigh possible difficulties.

All infants under 12 months of age with confirmed HIV infection should be started on ART, irrespective of clinical or immunological stage. For children age 12 months or older, clinical or immunological thresholds should be used to identify those who need to start ART. Severely malnourished children should - prior to take ART - benefit from nutritional rehabilitation.

Criteria to start ART				
Age	Infants <12 months	12 months through 35 months	36 months through 59 months	5 years or over
CD4%	All	<20	<20	<15
Absolute CD4[*]		<750 mm^3	<350 mm^3	As in adults (<200 mm)

The introduction of antiretroviral treatment (ART) in the mid-1990s led to a marked reduction in morbidity and mortality from HIV infection. In addition to improving quality of life and reducing AIDS related deaths, ART treatment has been recognized to prevent HIV transmission by reducing viral load (1).

However, over time ART has been associated with an increasing number of metabolic abnormalities such as the

development of dyslipidemia, insulin resistance, and HIV lipodystrophy syndrome (HIV-LS). These metabolic change are known to contribute for the development of cardiovascular disease (CVD) and diabetes mellitus (DM), representing a challenge in the treatment of HIV infection. Moreover, lipodystrophy body changes can jeopardize the quality of life of these patients, leading to low adherence to ART and subsequent virologic and clinical failure (2).

During the last decade, an increasing frequency of dyslipidemia has been observed among ART treated HIV-positive patients. The prevalence lays somewhere in between 20% and 80% including hypertriglyceridemia (40-80%) and high total cholesterol (10-50%), with at least one physical abnormality in approximately 50% of patients depending on the type of drug regimen used (3). It is reported that as high as 82.3% of first line ART and 76.9% pre-ART patients had at least one lipid profile abnormality (4).

Patients with human immunodeficiency virus (HIV) /acquired immunodeficiency syndrome (AIDS) frequently present alterations in lipid metabolism due to infection with HIV itself, including elevated serum concentrations of triglycerides and low levels of total cholesterol (5). The mechanisms responsible for lipid profile changes in HIV/AIDS infected patients are proven to be complex and to date are not fully understood but are probably multifactorial. It is suggested that various conditions and complex interactions involving the direct and indirect effects of antiretroviral medications and HIV infection itself have played a role in development of dyslipidemia (6). Lipid profile alterations in pre ART patients are associated to the host's response to systemic inflammation and persistent viral infection mediated by various cytokines including tumor necrosis factor (TNF), interleukins, and the interferon's secreted by active immune cells in the adipose tissue (7). Increased production of these cytokines and inflammatory responses enhance β-adrenergic stimulation of adipose tissue and thus advance adipose tissue lipolysis which in turn results in a secondary elevation in hepatic fatty acid levels, providing a stimulus for triglyceride synthesis and secretion as very-low-density lipoprotein (VLDL) particles (6).

Different ART classes and even individual agents within each drug class can have disparate effects on lipid profile alteration which may determine selection of ART regimens for initiations of treatment. However, most of the previous studies explored vigorously on the effect of old ART regimens like stavudine (d4T) in lipid metabolism, which are now almost excluded from the combination therapy. Still the effect of recently approved ART regimens like Tenofovir Disoproxil Fumarate (TDF) on lipid metabolism remains fully unexplained particularly in sub Saharan African where most of HIV patients live. In this region, where 8 to 71% of patients initiating ART die within the first year of treatment, apart from baseline CD4 count, viral load, and stage of the disease, dyslipidemia is thought to be one of the contributing variables to high AIDS-related mortality (8). In addition, patients in developing nation initiating ART may experience different rates and types of lipid abnormalities than patients in developed countries because of differences in genetic background, dietary intake, and lifestyle factors (9). A better understanding of the prevalence and patterns of lipid metabolic derangements at early stage in both HIV infected patients and those initiated ART could be important to identify potential interventions as well as additional clinical measurements that can be used to improve the care of HIV patients.

Methods and Materials

Selection of Patients

The study was conducted in the Dept. of Biochemistry and in collaboration with OBGY and Pediatrics Dept. at CCM Medical College Kachandur, Durg. Investigation was carried out in 70 patients ART treated group compared with 70 of naive group.

Study period and design

This study was done at Chandulal Chandrakar Memorial Medical College Kachandur, Durg. This is the largest and first private medical college in the CG state. A comparative cross sectional study design was used to assess the prevalence and patterns of lipid profile derangements among HIV patients receiving first line ART with respect to treatment naive groups at CCM Medical College from Sept. 2014 to December 2017.

Study populations

All adult HIV positive patients (≥18 years of age) visited CCM Medical College and Govt. ART center Durg from Sept. 2014 to December 2017, were our source population for cases and controls.

Cases were defined as adult HIV positive (≥18 years old) who had been on first line ART treatment continuously for at least six months duration and controls were HIV positive adults who were not yet receiving ART prior to time of data collection. Those who had started/changed first line ART treatment within less than six months' time and those on 2nd line ART treatment (for cases), with known diabetics and cardiovascular disease, those using lipid lowering drugs, Pregnant/ breast feeding womens, were excluded from the study.

First-line ART regimens

As defined by the WHO, regimens that included nucleoside reverse transcriptase inhibitors (NRTIs): 3TC, AZT, or d4T,

TDF, and nonnucleoside reverse transcriptase inhibitors (NNRTIs): NVP or EFV and or do not include PIs.

Data collection procedure

Clinical and demographic data collection: Information on sex, age, specific ART type in use , ART start date, duration of treatment, duration of HIV infection, BMI, relevant signs and symptoms and medications if any were collected by trained nurses using structured questionnaires and patients medical record.

Blood Sample Collection, Transport and Processing: Following a standard and safety collection procedure, about 5 ml fasting venous blood was taken from the patients and the control groups by clinical nurses and senior laboratory technologist. Sera were separated after centrifugation at 3000 rpm for 10 minutes, stored at -20°C and thawed just before analysis.

Laboratory investigations: Fasting serum samples were analyzed for total cholesterol (TC) (10), triglyceride (TG) (11), High Density Lipoprotein- Cholesterol (HDL-c) (12). Low density lipoprotein cholesterol (LDL) and Very low density lipoprotein (VLDL) was determined by Friedewald Equation (13).

Data Analysis

Data were expressed as mean ±SD. Mean values were assessed for significance by paired student –t test. A statistical analysis was performed using the Stastical Package for the Social Science program (SPSS, 23.0). Frequencies and percentages were used for the categorical measures. Probability values $p < 0.05$ were considered statistically significant.

Results and Discussion

Total 140 participants were selected for study. 50% participants were on first line ART cases and remaining 50% participants who were ART naive controls.

Table no 1 show General characteristics of the study population

Characteristics	ART treated group (n=70)	ART naive group (n=70)
	Group I	Group II
Age	8.84± 6.32	13.8±8.46
Sex Male	23	31
Female	47	39
Residence in town	29	32
Residence in Rural	41	38
< 18 underweight	13	10
18-25 normal weight	48	52
>25 overweight	9	8
Hypertension History	0	0

Lipid alterations in patients with HIV/AIDS caused by the infection itself had been reported before the implementation of ART. In this study we showed that , serum concentration of triglycerides , total cholesterol, LDL-c and VLDL-c were significantly increased and HDL-c were lower in HIV-seropositive patients receiving ART compared to ART naïve group controls. The finding of Nguemaïm NF and Fantoni M (14, 15) supports to our findings and shows the activity of HDL-c decreased found in group I. These alterations were detected in patients infected with different HIV-1 subtypes.

The concentration of HDL-c in group I patients were 29.85 ± 21.56 and in group II the activity were 40.37 ±23.56 but there is no significant difference found in both groups. Low serum concentrations of HDL-c can be used as a marker of chronic inflammatory activity. In a cohort study conducted in Spain, untreated HIV-infected patients presented low HDL-c levels, especially if they had already received antiretroviral therapy in the past.21 However, HDL-c levels were found to be low even in patients receiving ART presenting adequate viral suppression and immune reconstitution, a finding that suggests that inflammatory activity was not completely controlled (16).

There was statistically significant difference between the two groups for TC, TG, TC/HDL-c ratio and TG/HDL –c ratio. The TC/HDL ratio was > 5 in 6 (8.5%) of group II subjects and 19(27.1%) of group I with participants on ART being 4 times more likely to have higher TC/HDL-c ratio ≥5. A high triglyceride to HDL-C ratio (≥2.4), a strong indicator of the insulin resistance syndrome, was detected in 42.3% of group II participants and 60% of group I participants (p=0.04). There was no significant difference between the two groups on HDL-C<40 and LDLC >130 found. Pefura Yone et al. also found higher prevalence of raised value of TC, LDL-c, TG, and TC/HDL-c ratio > 5 in participants taking AZT compared to those taking D4T, while the prevalence of HDL<40 was similar in both regimens (17).

On the basis of our study we concluded that the level of TG, TC, HDL-c and VLDL-c is high in HIV positive populations

receiving first line ART (group I) as compared to ART naïve (group II). Considering that these altered lipid profiles can be an independent risk factors for coronary artery diseases and myocardial infarction, treatment with first-line ART may actually have potential risks for cardiovascular health of HIV positive people receiving ART. HIV-infected patients without ART presented lipid alterations associated with the infection itself, characterized by a decrease of total cholesterol, LDL-c, and HDL-c, and by an increase of triglyceride levels. In contrast, ART regimens promoted distinct alterations in the lipid metabolism of these patients.

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