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Determination of Lipid Derangements in Human Immunodeficiency Virus Patients Undergoing Anti-Retroviral Therapy

Qamar Bashir, Zujaja Hina Haroon, Naveed Asif*, Muhammad Qaiser Alam Khan, Eijaz Ghani, Syed Raza Jaffar**

Armed Forces Institute of Pathology/ National University of Medical Sciences (NUMS) Rawalpindi Pakistan, *Combined Military Hospital, Quetta/National University of Medical Sciences (NUMS) Pakistan, **Combined Military Hospital, Lahore/National University of Medical Sciences (NUMS) Pakistan

ABSTRACT

Objective: To determine lipid derangements in HIV-positive patients receiving anti-retroviral therapy (ART).
Study Design: Comparative cross-sectional study.
Place and Duration of study: Chemical Pathology Department, in cooperation with the Department of Virology at Armed Forces Institute of Pathology (AFIP), Rawalpindi Pakistan, from Mar 2019 to Mar 2020.
Methodology: In this study, two groups were made. In Group-1, lipid profile estimation was done in HIV patients without treatment. In contrast, lipid profile estimation was done after one year of treatment with anti-retroviral drugs in Group-2.
Results: One hundred and two HIV-positive subjects were included in our study. Of these patients, 88(86.27%) were males, and 14(13.73%) were females. Independent sample t-test revealed a statistically significant difference (p-value<0.05) in serum cholesterol, serum triglycerides, serum high-density lipoprotein (HDL-c), low-density lipoproteins (LDL) and very low-density lipoproteins (VLDL) between the two groups.
Conclusion: Hyperlipidemia in HIV patients getting anti-retroviral therapy (ART) exposes them to a high risk of coronary artery diseases and myocardial infarction. Hence lipid profile of patients getting ART must be regularly monitored, and hyperlipidemia, if present, should be managed.

Keywords: Acquired immunodeficiency syndrome (AIDS), Antiretroviral therapy (ART), Cholesterol, Human immunodeficiency virus (HIV), hyperlipidemia.

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INTRODUCTION

HIV-positive patients receiving ART are linked with extensively reported derangements in lipid profile.[1] Patients, especially receiving protease inhibitors (PI), are at risk of these changes during treatment. PIs are linked with derangements in the metabolism of glucose and lipids, and modification in the accumulation of fat in different parts of the body.[2] Owing to changes in lipid profile and abnormal glucose metabolism, chances of formation of plaques and atherosclerosis are increased. This results in a high risk of cardiovascular diseases and diabetes mellitus.[3] Pathophysiology of atherosclerosis in HIV comprises several elements, mainly involving direct endothelial injury and dysfunction. Derangements in lipid profile with nucleoside reverse-transcriptase inhibitors (NRTI), i.e., stavudine, have also been studied. However, NRTI is associated with very few changes.[4] There has been a variable outcome of ART on TG, HDL-c and LDL-c levels. The survival of patients with HIV has improved over the last ten years because of ART. With time, there has also been an increase in first-line ART regimens.[5-7]

Following the WHO guidelines, the first-line anti-retroviral regimen is widely used in Africa. This includes NRTI with an NNRTI. Unfortunately, there have been dangerous side effects of second-line anti-retroviral therapies on the lipid profile of patients. However, medicines have achieved wonderful results against HIV/AIDS.[8,9] Recent studies also demonstrate that major risk factors in HIV-positive patients on ART are responsible for lipid derangements. These factors include ART duration, age, sex, high BMI, smoking, alcohol intake, low CD4 cell counts, less physical activity, depression and dietary habits.

Even though lipid derangements are very common with ART, recent WHO guidelines do not include lipid profile monitoring in patients on ART. Furthermore, very insufficient data is available in favour of dyslipidaemia linked with ART in African countries.[10] Currently, in our setup, lipid profile measurements are not a common part of routine examination which is a prime criterion to increase the life expectancy of HIV infected patients and improve treatment outcome. Therefore, this study was planned to determine lipid derangements in HIV-infected patients undergoing ART in our setup.

Correspondence: Dr Qamar Bashir, Chemical Pathology, Armed Forces Institute of Pathology, Rawalpindi, Pakistan
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METHODOLOGY

This study was conducted at Chemical Pathology and Endocrinology Department in cooperation with Virology Department, Armed Forces Institute of Pathology, Rawalpindi Pakistan, on HIV-infected patients from March 2019 to March 2020. Institutional Ethical Review Committee approval was taken for the study (ERC ID: READ-IRB/20/461 dated 5 June 2020). 102 adult subjects of both genders aged 18 to 68 years were included in the study.

WHO sample size calculator was used to determine the sample size by taking a 95% confidence level and a margin of error of 5%. The overall prevalence of HIV in Pakistan is less than 1% in the adult population.[11]

Inclusion Criteria: All newly diagnosed HIV-positive patients were included in the study.

Exclusion Criteria: Patients with co-morbidities like cardiovascular disease, metabolic syndrome and lipid-lowering drugs were excluded from the study.

Subjects were selected through a non-probability consecutive convenient sampling technique after taking informed consent. Detailed clinical history was obtained. Two groups were made. In Group-1 (including 56 subjects), lipid profile estimation was done before the treatment. In comparison, in Group-2 (including 46 subjects), lipid profile estimation was done after one year of treatment with anti-retroviral drugs.

Samples were collected from HIV-infected patients after taking their written consent. The blood sample was drawn from each patient in a yellow-topped gel tube for cholesterol, triglycerides, HDL, LDL and VLDL-c after 10-12 hours of overnight fast. After taking all pre-analytic variables into account, samples were analyzed on a fully automated random-access discrete chemistry analyzer ADVIA 1800 by spectrophotometry. Calibration and patient results validation were done by internal quality control (IQC).

Statistical Package for Social Sciences (SPSS) version 23.0 was used for the data analysis. The Shapiro-Wilk test was used for analyzing the normality of data. Quantitative variables were expressed as mean and SD. An independent sample t-test was used for comparison between the two groups. The *p*-value lower than or up to 0.05 was considered as significant.

RESULTS

There were 102 HIV-positive patients included in our study. Of these patients, 88(86.27%) were males, and 14(13.73%) were females. Two groups were made based on anti-retroviral treatment or not. The mean age was 35.89±7.36 years for Group-1 and 38.08±8.37 years for Group-2 patients. The independent sample t-test was applied to find the difference in hyperlipidaemia between the two groups (Table). This showed a statistically significant difference in lipid profile parameters between the two groups. The outcome showed raised levels of serum cholesterol, TG, LDL-c and VLDL-c but decreased HDL-c levels among patients on ART for more than one-year duration. Hence this showed that ART might result in developing hyperlipidaemia.

Table: Difference of Biochemical Markers in Lipid Profile between the Groups (n=102)

Parameters	Study Groups		*p*-value
	Group 1 n=56 (Mean±SD)	Group 2 n=46 (Mean±SD)	
Age in years	35.89±7.36	38.08±8.37	-
Serum Total cholesterol	3.5±0.93	5.7±1.38	0.03
Serum Triglyceride (TG)	2.01±1.08	2.57±1.06	0.01
Serum Low density lipoproteins(LDL)	3.74±1.38	1.0±0.5	0.01
Serum High density lipoproteins(HDL)	1.01±0.2	0.8±0.23	0.01
Serum Very low-density lipoproteins(VLDL)	0.92±0.50	1.16±0.48	0.02

DISCUSSION

Multiple diseases are associated with hyperlipidaemia. These diseases may be of genetic origin or other multiple linked diseases like diabetes and cardiovascular. Serum cholesterol, TG, LDL-c and VLDL-c, and variable levels of HDL-c and Apo-B are affected and deranged after the use of ART. In view of previous studies' perspective, our study shows the same results of the effects of ART duration on hyperlipidemia directly. The different meta-analysis also revealed a higher chance of hyperlipidemia among the HIV-infected patients using ART as compared to patients not using ART.[12-14]

A study by Pefura Yone *et al.*[15] in 2011 showed similar results to ours. Overall, 276 patients were selected for the study, and it revealed that ART has a strong association with elevated levels of total cholesterol and LDL-c. Similarly, a study by Tadewos *et al.*[16] in 2012 revealed that ART was linked with increased total cholesterol and LDL-c but no significant

difference in HDL-c. Finally, Nsagha *et al.*[17] in 2015 in their study showed similar results as ours.

Due to medium to long exposure to ART affecting lipid metabolism, lipid profiles have induced changes. ART is directly involved in changing lipid metabolic processes and has also affected mitochondria, endothelial and adipocyte cell function. These changes have been suggested for altered lipid profiles.[18] Increased cholesterol levels and TG may be the reason for increased very-low-density lipoprotein (VLDL) and decreased TG clearance. Lipid peroxidation and oxidative stress linked with HIV/AIDS before the use of ART for HIV may cause mild lipid profile derangements.[19] Cytokines of various types, including tumour necrosis factor (TNF), interferons and interleukins may mediate the host's response against infection and may lead towards decrease HDL-c and increase serum TG levels.[20-22]

CONCLUSION

Hyperlipidaemia in HIV patients receiving ART exposes them to a high risk of coronary artery diseases and myocardial infarction. Hence lipid profile of patients getting ART must be regularly monitored, and hyperlipidaemia, if present, should be managed.

Conflict of Interest: None.

Authors' Contribution

Following authors have made substantial contributions to the manuscript as under:

QB & ZHH: Data acquisition, data analysis, drafting the manuscript, critical review, approval of the final version to be published.

NA & MQAK: Conception, Study design, drafting the manuscript, approval of the final version to be published.

EG & SRJ: Data interpretation, critical review, drafting the manuscript, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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