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Dyslipidemia and fasting glucose impairment among HIV patients three years after the first antiretroviral regimen in a Brazilian AIDS outpatient clinic

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ABSTRACT

Objective: To evaluate the cumulative incidence of dyslipidemia and fasting glucose impairment three years after initiating the first antiretroviral (ART) regimen and the association with the type of ART regimen in an AIDS outpatient clinic in Brazil.
Methods: Retrospective cohort of HIV-1 infected patients attending an outpatient HIV clinic in Vitoria, Brazil, between January/2010 and May/2011. Data, including blood pressure, dyslipidemia (high total cholesterol and low HDL-C), fasting glucose, and cardiovascular risk by Framingham Risk Score were abstracted from medical records from clinic visits six months prior and three years after starting ART. We assessed independent associated factors for dyslipidemia using multiple logistic regression.
Results: Four hundred and ninety-eight patients on ART were studied. Median age was 45 years (interquartile range (IQR): 37–52), and median time since HIV diagnosis was 7.7 years (IQR: 3.8–10.0). The proportion of patients with dyslipidemia was 22.3% (95% CI: 18.6–25.9%) 36 months after ART initiation. Triglycerides levels >150 mg/dL (55.2% vs. 25.4%, $p = 0.021$) and high fasting glucose (5.8% vs. 2.3%, $p = 0.034$) were diagnosed more frequently after ART use when compared to baseline values. Multiple logistic regression analysis has shown dyslipidemia to be associated with lopinavir/r use [OR = 1.74 (95% CI: 1.12–2.86)].
Conclusion: These data show high chance of dyslipidemia after initiation of ART. Long-term follow-up will help identify the impact of ART on cardiovascular risk.

Introduction

AIDS associated morbidity and mortality has substantially declined since the widespread use of highly active antiretroviral therapy (ART). Data from Brazil were among the first to show this finding.[1] Survival time has increased significantly among adult Brazilian AIDS patients, which demonstrates the benefits of universal access to antiretroviral treatment in a developing country. On the other hand,

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non-AIDS conditions are emerging as significant causes of morbidity and mortality in the HIV-infected population. Increased rates of dyslipidemia and diabetes have been well documented,[2,3] with multiple factors accounting for these findings, especially the use of antiretroviral drugs. HIV infection itself has been associated with decreases in low-density lipoprotein (LDL) and high-density lipoprotein (HDL) cholesterol, and progressive appearance of hypertriglyceridemia, likely related to Interferon alpha (IFNα) circulating levels in later stage disease.[4] A significant association between decreasing CD4+ cell count and decreasing levels of HDL has been described, as well as an association between a history of AIDS-defining events and higher total cholesterol and triglyceride concentrations.[2]

The incidence of diabetes mellitus in HIV-infected men with ART exposure has been shown to be over four times than that seen in HIV-negative men in the Multicenter AIDS Cohort Study,[5] after adjusting for body mass index and age. Insulin resistance has been reported in 13% of HIV-infected patients after a year of ART in a prospective observational cohort study.[6] In HIV-infected women, diabetes mellitus incidence has been shown to be associated with and longer cumulative exposure to nucleoside reverse transcriptase inhibitors (NRTI).[7]

As non-AIDS morbidity has became more significant in recent years, there has been speculation whether HIV infection may be a marker for higher cardiovascular risk, or exposures unrelated to HIV or ART.[8] HIV-infected patients, for example, usually have higher smoking rates, and usually need assistance to quit.[8–10]

Brazilian national guidelines for ART therapy in adults[11] recommend routinely estimation of cardiovascular risk by use of Framingham Risk Score (FRS). Estimation of the risk for a cardiovascular event in ten years by the FRS is based on age, total cholesterol, HDL-cholesterol, systolic blood pressure and smoking status.[12] It is designed for patients aged 20 years and older who do not have heart disease or diabetes. As few studies have reported the prevalence of these metabolic complications in our country,[13–15] the aim of our study was to evaluate the cumulative incidence of dyslipidemia and fasting glucose impairment three years after starting ART and to investigate the association between ART and dyslipidemia in an AIDS outpatient clinic in Brazil.

Methods

This was a retrospective cohort study of HIV-1 infected adult patients (18 years and older) attending an AIDS outpatient clinic at a University Hospital in Vitória, Brazil, between January 2008 and May 2011. This clinic is the second largest Specialized Assistance Service (SAS) in the city of Vitoria, working since the 1980s and is part of the national public network providing care for HIV-infected patients in Brazil.

Six hundred and seventy-nine patients were followed in this outpatient clinic during the study period. A total of 164 were excluded due to unavailability of lipid, glucose or FRS results before treatment, diagnosis of dyslipidemia before starting ART, or lost to follow-up. The majority of the excluded patients were aged less than 30 years and thus no lipid profile had been requested. The remaining 515 patients were included.

Demographic, behavioral and clinical data including blood pressure measurements, total and HDL cholesterol, fasting glucose, and FRS were abstracted from medical records and interviews with all patients, from the last visit (3–6 months) prior to and three years following initiation of ART. Information on time on ART, type of ART, smoking status, and lipid lowering therapy was also collected. LDL-cholesterol was calculated using Friedwald's formula in individuals with triglycerides $\leq$400 mg/dL. When TGL >400, LDL cholesterol was not available.

Blood samples were collected after 12 h fasting, according to the usual laboratory protocol. All patients included in the analyses were on antiretroviral therapy according to Brazilian Consensus of Antiretroviral Therapy for Adults guideline.[11] Only patients on their first ARV regimen were studied. In case of ARV regimen change the regimen used for at least 70% of the study period was considered.

Results of HDL-cholesterol were stratified as normal or low (<40 mg/dL in men and <50 mg/dL in women); total cholesterol was deemed normal or high (>200 mg/dL), LDL cholesterol as normal or high (>160 mg/dL), and triglycerides as normal or high (>150 mg/dL), according to the Brazilian Cardiology Society guidelines.[16] Impaired fasting glucose and diabetes were defined if measurements of fasting glucose levels were >99 mg/dL and >126 mg/dL, respectively. Patients with low HDL cholesterol and high total cholesterol levels were grouped as having "dyslipidemia".

Patient data were entered into a database and analyzed using SPSS, version 17 for Windows (Chicago, IL, USA). Standard descriptive analyses were performed including frequency distributions for categorical data and calculation of medians and interquartile ranges for continuous variables. Univariate analyses to assess factors associated with dyslipidemia were tested using Chi-square and Fisher's Exact Test, and *t*-test and analysis of variance were used for testing differences between means. Odds ratio (OR) was used as a measure of association, estimated with a 95% CI. Independent risk factors for "dyslipidemia" were assessed through multiple logistic regression with 15% as the critical *p*-value for variable entry and 10% as the criterion for variable elimination.

The study protocol was submitted and approved by the Escola de Ciências da Saúde da Santa Casa de Misericordia institutional review board (# 048/2007).

Results

Five hundred and fifteen (72.1%) patients on ART had lipid and glucose data available before and after ARV treatment and were included in the study. Among them 17 (3.3%) had been diagnosed with dyslipidemia before ART and were not included. Of the remaining 498 patients, 309 (58.9%) were male and 301 (60.4%) Caucasian. Median age was 45 years at 2010/2011 visit (interquartile range [IQR]: 37–52), and median time since HIV diagnosis was 7.7 years (IQR: 3.8–10.0). The cohort's median age is few years older than the usual age in our region as many young patients had no lipid profile measured before ART. The cumulative incidence of dyslipidemia