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Original article

Impaired lipid profile and insulin resistance in a cohort of Austrian HIV patients

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ABSTRACT

Introduction: Traditional risk factors for cardiovascular diseases have been shown to have an even higher impact in the HIV infected population. Cardiovascular risk factors amongst people living with HIV treated in doctor's offices in Austria have not been documented before. Our study aimed to close this gap, focusing on dyslipidemia, diabetes mellitus and diabetes risk.
Patients and methods: After ethics approval, consecutive patients who visited their treating physicians for routine checks were enrolled. The lipid profile was assessed by measuring total cholesterol, triglycerides, HDL and apolipoprotein B and calculating LDL and non-HDL-cholesterol. The diabetes risk was calculated by measuring insulin and blood glucose levels and assessing insulin resistance and beta cell function using the HOMA-IR model.
Results: 522 patients were included in the analysis. 90.2% of the participants were on antiretroviral therapy. Two third had an impaired lipid profile, but dyslipidemia had been diagnosed only in 46.3% of the patients. There was a clear correlation between protease inhibitor use and pathologic blood lipids. Of the persons with dyslipidemia, 18.4% received lipid lowering drugs. 8 persons (1.6%) fulfilled the criteria for diabetes mellitus. Of those, 4 patients already had a diagnosed diabetes mellitus. 50.1% of the study participants showed an increased insulin resistance. Patients on nucleoside reverse transcriptase inhibitors had significantly higher markers for impaired glucose metabolism.
Discussion: We found a high percentage of increased insulin resistance, of impaired lipid profile and in contrast to this a low treatment rate with lipid lowering drugs in this cohort of people living with HIV.

1. Introduction

The introduction of highly active antiretroviral therapy (HAART) and the availability of an armamentarium of potent antiretroviral substances have improved the prognosis for people living with HIV (PLWHIV) dramatically. As a consequence, the mean age of PLWHIV in countries with access to modern therapies is increasing [1]. The median age of Austrian HIV patients today is 45.4 years, 11.4% of the patients are older than 60 years [2]. As in the non-infected elderly population, diabetes mellitus (DM) and cardiovascular events are common in the ageing HIV infected population and show increasing mortality rates relative to AIDS defining diseases [3–5].

Cardiovascular events, the leading cause of death in high income countries, are even more common in PLWHIV than in non-infected control groups [6,7]. The reason may be found in the accumulation of several risk factors, of which some are attributed to the chronic viral infection itself, like immune dysfunction and chronic inflammation, some to side effects of antiretroviral drugs, like dyslipidemia [7]. Traditional risk factors for cardiovascular diseases like smoking, elevated lipids and DM have been shown to have an even higher impact in the HIV infected population [7].

Metabolic changes are common in PLWHIV and likely play a role in the development of atherosclerosis. An increased rate of

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dyslipidemia in HIV infected populations has been documented and may relate to effects of HIV as well as antiretroviral therapy (ART). Triant et al. showed that dyslipidemia was the cardiac risk factor most strongly associated with acute myocardial infarction (AMI) among PLWHIV, when adjusted for age, race, gender, and other cardiac risk factors [8].

The other important factor that severely contributed to the increase in AMI rates in the HIV group was DM [8]. Several studies showed high rates of DM in PLWHIV, especially under ART. Brown and colleagues found in the Multicenter AIDS Cohort Study a 14% prevalence rate of DM in HIV-infected men using ART compared with 5% in seronegative men. The incidence of DM in HIV-infected men with HAART exposure was more than 4 times higher than that of HIV-seronegative men [9]. In the ageing HIV population that is also on ART, DM rates are expected to increase even more in the future [10].

Thus, for reducing cardiovascular morbidity and mortality, it seems to be very important to screen and, if necessary, treat every HIV positive patient on a regular basis for cardiovascular risk factors. This is, however, not always the case in HIV treatment facilities in daily routine.

Approximately 1000 PLWHIV in Austria (20% of all Austrian HIV-patients) are not treated in the hospital outpatient clinics but in doctor's offices of registered physicians. These physicians – 2 general practitioners and 2 dermatologists – form together the ÖGNÄ (Österreichische Gesellschaft Niedergelassener Ärzte, translated: Austrian society for registered doctors)-HIV-cohort [11].

The ÖGNA-HIV-physicians perform routine visits with their HIV infected patients every 3–6 months. Cardiovascular risk factors amongst this HIV population have not been documented before with the exception of smoking, which has been subject of a recent study [12]. Our study aimed to close this gap, focusing on dyslipidemia, DM and diabetes risk.

2. Patients and methods

This epidemiologic evaluation was conceptualized to document real life major cardiovascular risk factors of patients in the ÖGNÄ-HIV-cohort.

It was a national survey encompassing consecutive patients who visited their treating physicians for routine checks. All ÖGNÄ-HIV physicians participated in the evaluation.

Consecutive patients who visited their treating physician for routine control were included in this evaluation. Inclusion criteria were: Age ≥18 years, documented HIV-Infection and written informed consent for participation obtained from the subject.

The lipid profile was assessed by measuring total cholesterol, triglycerides, HDL and apolipoprotein B in the fasting state. LDL was calculated using the formula of Friedewald: [LDL-cholesterol] = [total cholesterol] – [HDL-cholesterol] – [triglycerides]/5.

Additionally, non-HDL-cholesterol (Non-HDL-C) was calculated as total cholesterol – HDL. As the Friedewald formula does not work in case of triglycerides >300, in these patients only Non-HDL-C was used. Impaired lipid profile was computed (according to a consensus statement of Austrian societies involved in this field) as either having an LDL-level > 130 mg/dl OR an HDL-level < 40 mg/dl OR a triglyceride level > 150 mg/dl.

The diabetes risk was calculated by measuring insulin and blood glucose levels, assessing insulin resistance and beta cell function with these parameters.

The diabetes risk of the patients was assessed using the HOMA-IR Model:

HOMA-IR (Homeostasis Model Assessment for Insulin Resistance)

HOMA-IR = fasting plasma glucose (mmol/l) × fasting insulin (μU/ml)/22.5

A value >2.0 was considered insulin resistance (women > 35 years: >2.6)

Additionally, the following parameters were documented:

- Patient characteristics obtained from the patients' charts (sex, year of birth, smoking status, known cardiovascular risk factors: dyslipidemia, diagnosed diabetes, hypertension, history of cardiovascular events; time since infection with HIV, time since initiation of HAART, CD4 nadir and time since CD4 nadir; HIV stadium)
- Lipid profile (total cholesterol, triglycerides, HDL, apolipoprotein B, LDL, Non-HDL-cholesterol)
- Medications (current medication for the treatment of HIV, current medication for dyslipidemia, current medication for diabetes, current medication for other co-morbidities)

The enrollment period had a duration of 6 months, from May to November 2013. Before the start of the study ethics approval was obtained from the local ethics committee (EK 12-252-VK). After the enrollment period source data verification was performed to test the data quality.

2.1. Statistical analysis

All metric variables (LDL-cholesterol, total cholesterol, HDL-cholesterol, triglycerides, apolipoprotein B, and insulin level) were analyzed with means and standard deviation, when normal distributed. For group comparisons of means, the t-test was applied. Categorical variables (subjects with impaired lipid profile, subjects with diabetes mellitus, subjects with diabetes risk, subjects with risk for fatal CVD in different risk categories, subjects with lipid lowering medication, and subjects with diabetes medication) were documented with number of subjects, and percentages. For group comparison of categorical variables, the Chi^2-test was applied. Furthermore, we calculated a binary logistic regression model with dyslipidemia as the dependent and drug substance classes, smoking status, age, and sex as independent variables. In this analysis, age was used as a metric, and all other independent variables as categorical variables. Results are reported as odds ratios with 95% confidence intervals.

3. Results

522 patients were included in the analysis. The majority of them were CDC stadium A, the mean duration of the HIV infection was 8 years (ranging between 4 months and 30 years). 455 persons were on combined antiretroviral therapy (cART), mean duration of antiretroviral therapy was 5.5 years (range between 1 month and 23 years) (See Table 1 for more patient characteristics).

The results for the cardiovascular risk factors assessed are listed in Table 2. It shows that almost half of the patients were smokers and two third had an impaired lipid profile. Of note, only 46.3% of the patients had been diagnosed to have dyslipidemia before this evaluation (as declared by the physicians in the CRF). Of the persons with dyslipidemia, 18.4% received lipid lowering drugs, mostly statins, fibrates or ezetimibe (76.4%, 20.8% and 2.7%, respectively).

Concerning the parameters for DM, 8 persons (1.6%) fulfilled the criteria for DM. Of those, 4 patients (0.8%) already had a diagnosed DM, 3 (0.6%) were on treatment. 50.1% of the study participants showed an increased insulin resistance, according to HOMA-IR.