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Original article

Prevalence and risk factors of mild chronic renal failure in HIV-infected patients: influence of female gender and antiretroviral therapy

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ABSTRACT

Background: In people living with HIV, much is known about chronic kidney disease, defined as a glomerular filtration rate under 60 mL/min. However, there is scarce data about prevalence and risk factors for milder impairment (60–89 mL/min).

Objective: The present study aims to assess the influence of sex, antiretroviral therapy, and classical risk factors on the occurrence of mild decreased renal function in a large Spanish cohort of HIV-infected patients.

Methods: Cross-sectional, single center study, including all adult HIV-1-infected patients under antiretroviral treatment with at least two serum creatinine measures during 2014, describing the occurrence of and the risk factors for mildly decreased renal function (eGFR by CKD-EPI creatinine equation of 60–89 mL/min).

Results: Among the 4337 patients included, the prevalence rate of mildly reduced renal function was 25%. Independent risk factors for this outcome were age older than 50 years (OR 3.03, 95% CI 2.58–3.55), female sex (OR 1.23, 95% CI 1.02–1.48), baseline hypertension (OR 1.57, 95% CI 1.25–1.97) or dyslipidemia (OR 1.48, 95% CI 1.17–1.87), virologic suppression (OR 1.88, 95% CI 1.39–2.53), and exposure to tenofovir disoproxil-fumarate (OR 1.67, 95% CI 1.33–2.08) or ritonavir-boosted protease-inhibitors (OR 1.19, 95% CI 1.03–1.39).

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Conclusions: Females and patients over 50 seem to be more vulnerable to renal impairment. Potentially modifiable risk factors and exposure to tenofovir disoproxil-fumarate or ritonavir-boosted protease-inhibitors are present even in earlier stages of chronic kidney dysfunction. It remains to be determined whether early interventions including antiretroviral therapy changes (tenofovir alafenamide, cobicistat) or improving comorbidities management will improve the course of chronic kidney disease.

Introduction

In most countries with broad access to antiretroviral therapy, chronic kidney disease (CKD) in people living with HIV infection is now more likely to be the result of non-HIV associated conditions,[1,2] and it might have a higher prevalence and earlier onset than in age-matched uninfected individuals.[3–5] Although there is a low overall risk of developing end-stage renal disease,[6,7] decreasing GFR is related to a significantly increased risk of cardiovascular events and mortality.[8,9]

Even patients with milder grades of renal dysfunction already have sizable medical costs that can be attributed to renal function impairment.[10] Moreover, a considerable number of the antiretroviral drugs and antibiotics undergo renal elimination and demand dose-adjustments according to kidney function.[11] Lastly, the increasing exposure to some antiretroviral drugs can lead to progression to kidney disease, even in individuals with initially normal renal function.[12] Therefore, in clinical practice, it is important for the attending physician to identify the presence of incremental baseline risk factors and intervene where they are potentially modifiable and as early as possible.

Several studies have already been published evaluating the presence of risk factors for CKD stage ≥3.[7,13–18] However, there is a lack of information regarding the factors associated with earlier stages of renal dysfunction, also associated with increased risk of complications,[9,19] but in which preventive actions would be more feasible.

The aim of the present study is therefore to assess the influence of sex, type of antiretroviral therapy (ART), and the classical risk factors on mildly decreased renal function (CKD EPI eGFR 60–89 mL/min/1.73 m^2) among an urban population of stable patients with HIV-infection in a large Spanish cohort.

Methods

Study design

This was an observational, cross-sectional, single center study. The study project was reviewed and approved by the Institutional Review Board (CEIC Hospital Clinic i Provincial, Barcelona, Spain, IRB# 2014/1080). Eligible patients were all adult HIV-1-infected patients (>18 years old) with at least two serum creatinine measures during the calendar year of 2014. A description of the prevalence of the various stages of CKD of the entire cohort was published elsewhere.[20] For the current analysis, patients were excluded if they presented an estimated GFR above 181 mL/min/1.73 m^2, a diagnosis of chronic kidney disease (eGFR < 60 mL/min per 1.73 m^2), dialysis and/or kidney transplantation, or if they were recipients of a hepatic allograft.

The main objectives of our study were to describe the occurrence of mildly decreased renal function, defined as two consecutive measures of eGFR between 60 and 89 mL/min/1.73 m^2 over at least three months, and to determine the variables associated with a higher risk of this event. eGFR was obtained using the CKD-EPI creatinine equation.[21] As in other publications, we considered the African-American coefficient factor as not applicable to black patients from Africa, Europe and Antilles.[22,23]

The following demographic, clinical and laboratory parameters were abstracted from the HIV clinical database: age, sex, race, body mass index, hypertension (use of anti-hypertensive medication at CKD diagnosis), diabetes mellitus (glucose intolerance requiring pharmacological intervention), hyperlipidemia (use of hypolipidemic medication at CKD diagnosis), prior cardiovascular event, viruses, time of HIV-infection diagnosis, mode of transmission, AIDS stage, CD4 and viral load (current and nadir), current and previous antiretroviral treatment, hepatitis B coinfection (positive serology) and hepatitis C coinfection (positive serology + detectable HCV-RNA). Urinalysis for proteinuria was not available for the present study.

Data analysis

Demographic, clinical and laboratory parameters were described for patients with and without mildly decreased renal function. Quantitative variables were expressed as median and interquartile range. Analysis of normality of quantitative variables was performed using the Kolmogorov–Smirnov test, and because none of them displayed a normal distribution, nonparametric tests were used to compare these variables. Categorical variables were expressed as number, percentage, and 95% CI; the Chi-square test was used for comparisons. For all tests, statistical significance is considered if the p-value < 0.05. To identify risk factors associated with mildly decreased renal function, we performed a stepwise binary logistic regression analysis. Variables included in the model were those with a p-value < 0.05 in univariate analysis, or those considered relevant by other published studies. Statistical analyses were performed using the Predictive Analytics Software Statistics for Windows, v21.0 (SPSS Inc, Chicago, IL).

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