HIV infection is independently associated with chronic kidney disease and mild glomerular hyperfiltration, particularly in those of African descent

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Background

HIV-infected individuals are at increased risk of chronic kidney disease (CKD).[1] Traditional risk factors as well as those related to HIV infection and exposure to antiretroviral therapy (ART), particularly tenofovir disoproxil fumarate (TDF), may all contribute.[2]

[1] Yombi JC et al, HIV Medicine 2015; [2]Yombi JC et al, AIDS 2014

Methods

Study population

HIV-1 infected and uninfected AGE$_h$IV Cohort Study participants, aged ≥45 yrs.

Aims

To cross-sectionally compare the prevalence of a low estimated glomerular filtration rate (eGFR), albuminuria and proximal renal tubular dysfunction (PRTD) between HIV-infected and uninfected study participants.

To compare longitudinal eGFR decline during a follow-up up to 4 years (baseline, 2 biennial study visits) in HIV-infected individuals on cART.

Definitions

Low eGFR: eGFR below 60 ml/min, calculated using the CKD Epidemiology Collaboration formula

Albuminuria: urine albumin-creatinine ratio >3mg/mmol.

PRTD: urine retinol-binding protein:creatinine ratio >2.93µg/mmol and/or fractional phosphate excretion >20% with plasma phosphate <0.8 mmol/L

Statistical analyses

Multivariable logistic and linear regression analyses: to assess independent associations between HIV-status and a low eGFR, albuminuria and PRTD, adjusting for traditional CKD risk factors (listed below).

Linear mixed effects models to estimate eGFR decline over 4 year follow-up.

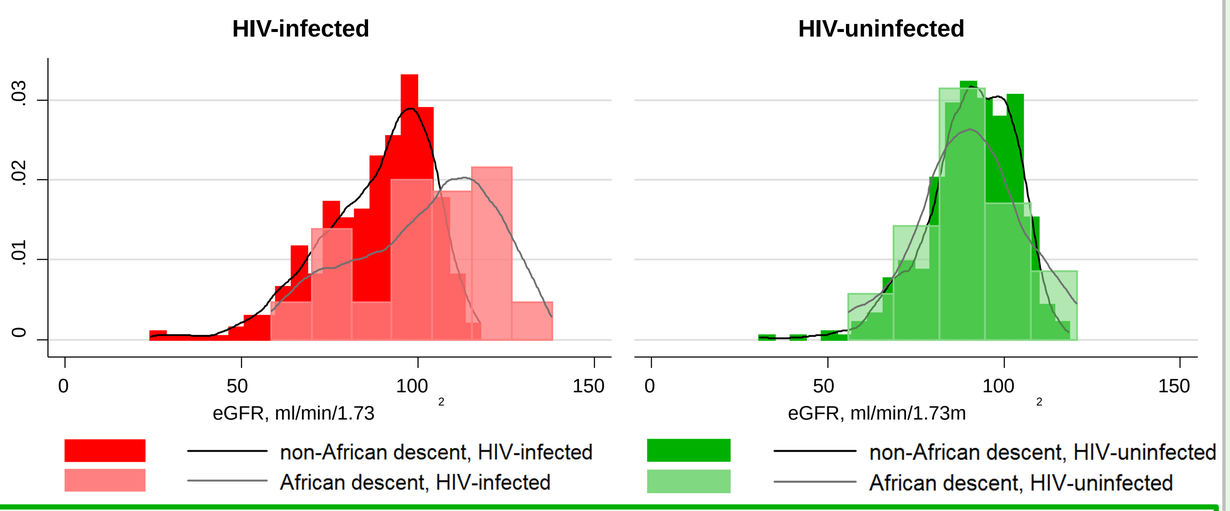
Multiple imputation was performed to handle missing baseline covariates.

Baseline characteristics

	HIV-infected, n=596 % or median (IQR)	HIV-uninfected, n=544 % or median (IQR)
age, years	52.7 (48.3 – 59.4)	52.1 (47.9 – 58.1)
male gender	87.9%	84.7%
African descent[1]	14.3%	6.4%
current / past smoking	32.1% / 35.1%	24.8% / 38.9%
chronic HCV infection[2]	3.5%	1.1%
diabetes mellitus[3]	6.7%	4.8%
hypertension[4]	50.2%	37.3%
LDL-C, mmol/L / using statin	3.1 (2.5 – 3.7) / 14.1%	3.3 (2.7 – 3.9) / 7.8%
using cART	95.0%	
regimen containing TDF	73.3%	

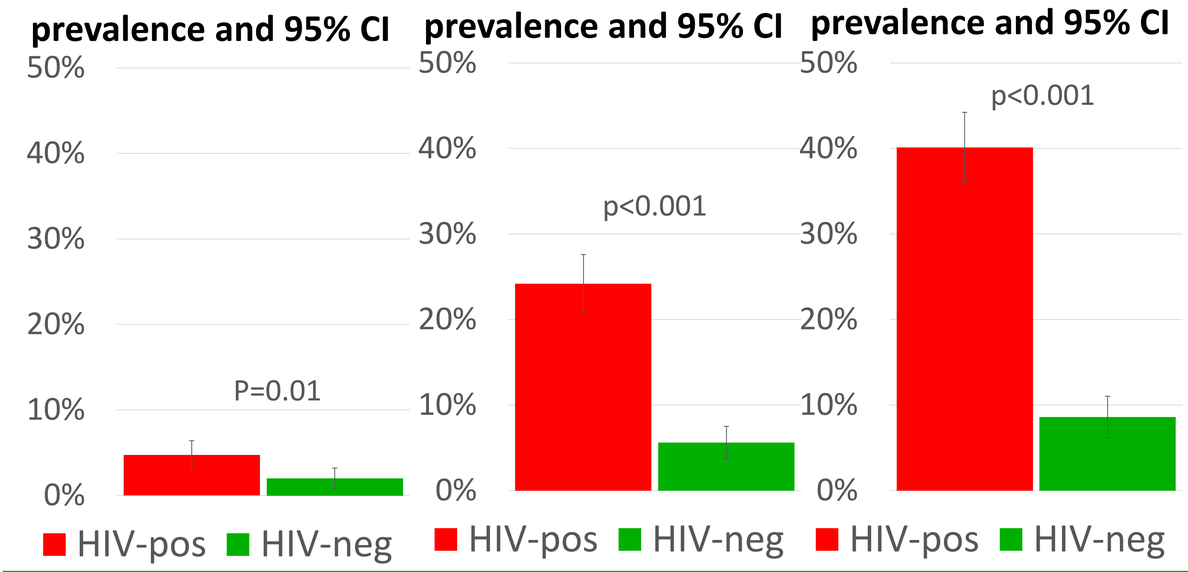
HCV, hepatitis C virus; LDL-C, low-density lipoprotein cholesterol; cART, combination antiretroviral therapy; TDF, tenofovir disoproxil fumarate. [1]birth country Suriname(Creole)/Netherlands Antilles/sub-Saharan Africa and/or invalid AGEreader measurement due to low reflection; [2]detectable hepatitis C virus RNA; [3]HbA1c ≥48 mmol/mol and/or blood glucose (fasting/non-fasting) ≥11.1/≥7.0 mmol/L and/or use of antidiabetic drugs; [4]mean systolic/diastolic blood pressure ≥140/≥90 and/or use of antihypertensive drugs.

Baseline eGFR distribution



- Median eGFR **not significantly different** between HIV-infected (92.6 ml/min, 95% CI 78 – 101) and uninfected individuals (91.3 ml/min, 95% CI 84 – 100), p=0.97
- More **extreme** low and high **eGFR values** in the HIV-infected study group
- Particularly **high eGFR** was observed in HIV-infected individuals of **African** descent

Baseline low eGFR, albuminuria and PRTD



HIV infection independently[#] associated with:

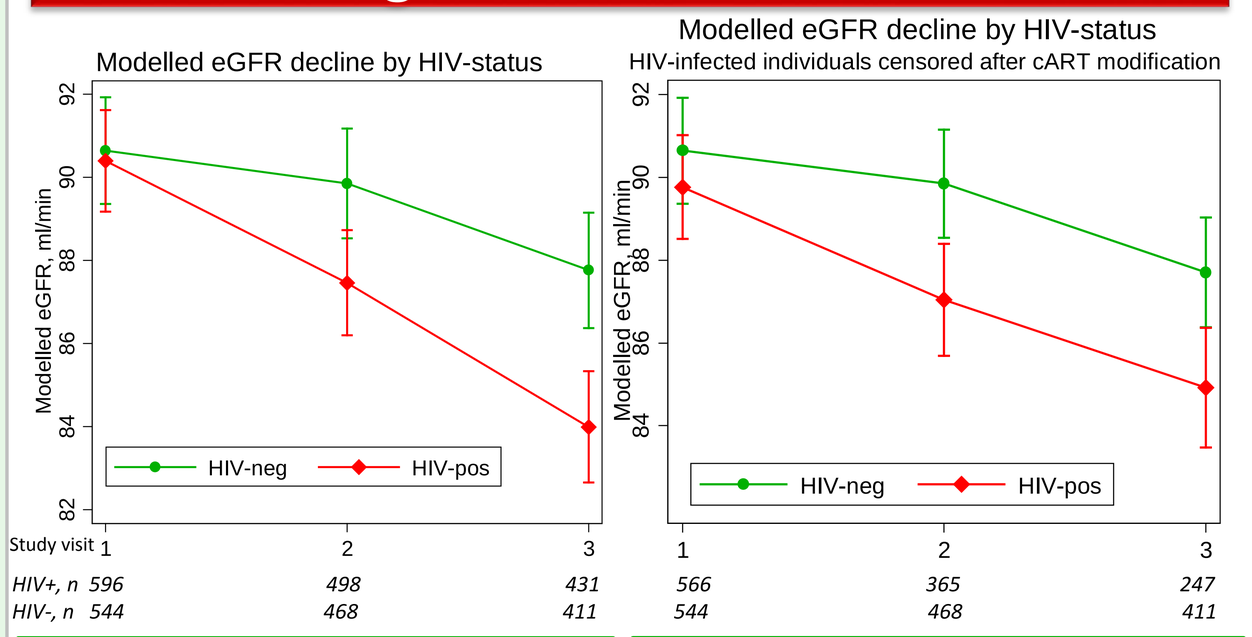
Low eGFR	Albuminuria	PRTD
OR_{HIV} 2.1 (95% CI 1.0 – 4.4)	OR_{HIV} 5.8 (95% CI 3.7 – 9.0)	OR_{HIV} 7.1 (95% CI 4.9 – 10.2)

Within the HIV-positive group:

- **cumulative duration of TDF exposure** independently associated with PRTD (OR 1.2 per year, 95% CI 1.1 – 1.3)
- **historic** but not current **TDF exposure** borderline independently associated with low eGFR (OR 3.3, 95% CI 0.9 – 11.4).

[#]adjusted for age, gender, ethnicity, smoking status, HCV infection, diabetes mellitus, hypertension, LDL-cholesterol, and use of statins

Longitudinal eGFR decline



Treated HIV infection independently[#] associated with 0.89 mL/min greater yearly eGFR decline (95% CI 0.58 to 1.20 mL/min, P<0.001).

HIV infection on stable cART independently[#] associated with 0.57 mL/min greater yearly eGFR decline (95% CI 0.25 to 0.88 mL/min, *P*<0.001).

[#]adjusted for age, gender, ethnicity, smoking status, HCV infection, diabetes mellitus, hypertension, LDL-cholesterol, and use of statins

Conclusions

In this cohort of middle-aged HIV-positive and HIV-negative individuals, the majority on TDF containing ART, **HIV was independently associated with prevalent low eGFR, albuminuria and proximal renal tubular dysfunction**.

Both **very low and high eGFR values** were more common in HIV-positive individuals, with higher eGFR particularly associated with being of African descent. This could be an expression of **glomerular hyperfiltration**, a condition associated with increased risk for CKD development. This suggests that **HIV-positive individuals of African descent** might be at **increased risk to progress towards CKD** despite currently having high eGFR.

Furthermore, treated HIV infection was independently associated with **greater eGFR decline** during a follow-up period up to 4 years. To a large extent, the high prevalence and progression of CKD may be due to the frequent and long-term use of TDF in this population.

Correspondence and funding

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