REGION

The prevalence of impaired renal function in well-treated people living with HIV is low but remains higher than in uninfected controls

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BACKGROUND

Reduced kidney function is an important non-AIDS comorbidity, with a reported prevalence of up to 24 % in people living with HIV (PLWH) [1-3]. Previous studies are focused in populations at increased risk of kidney disease, such as those with uncontrolled HIV infection, of African descent or with hepatitis C (HCV) coinfection.

We aimed to:

- Determine the prevalence of reduced kidney function in well-treated PLWH and in matched uninfected controls.

- Determine if HIV is independently associated with reduced kidney function

Table 1

Characteristics	PLWH	Uninfected controls	PLWH with eGFR ≤60 ml/min/1.73 m²
	n=598	n=2598	n=21
Age, median (IQR)	51 (44-60)	51 (44-60)	72 (67-75)
Sex (male), n (%)	530 (89.1)	2313 (89.1)	15 (72)
Ancestry, n (%)			
— Danish	551 (92.1)	2414 (94.1)	18 (86)
— Other Scandinavian	47 (7.9)	152 (5.9)	3 (15)
BMI (kg/m²), median (IQR)	24 (22-27)	26 (24-29)	23 (20-27)
Pack-years, median (IQR)	19 (8-33)	15 (6-26)	19 (15-40)
Diabetes, n (%)	27 (4.6)	99 (3.8)	4 (19)
Hypertension, n (%)	266 (46.0)	1458 (56.8)	18 (86)
Smoking, n (%)			
— Current	178 (29.8)	343 (13.2)	1 (5)
— Former	219 (36.6)	958 (36.9)	12 (57)
— Never	194 (32.4)	1288 (49.6)	8 (38)
Educational level after high school, n (%)			
Biomarkers			
Serum creatinine, mg/dl, median (IQR)	83 (76-92)	82 (75-89)	111 (94-129)
eGFR*, ml/min/1.73m², median (IQR)	89 (78-100)	91 (82-100)	56 (48-58)
eGFR* ≤60 ml/min/1.73 m², n (%)	21 (4)	43 (2)	21 (100)
eGFR* level, ml/min/1.73 m², n (%)			
— >90	291 (48.7)	1402 (54.0)	0 (0)
— 60-90	286 (47.9)	1154 (44.4)	0 (0)
— 45-59.9	16 (2.7)	39 (1.5)	16 (76)
— 30-44.9	4 (0.67)	4 (0.15)	4 (19)
— <30	1 (0.17)	0 (0.0)	1 (5)

Table 1. Clinical characteristics.
*using CKD-EPI formula
Abbreviations: BMI, body mass index; IQR, interquartile range; SD, standard deviation.
eGFR, estimated glomerular filtration rate.

METHODS

Scandinavian PLWH, virologically suppressed on combination antiretroviral treatment, without intravenous drug use, or HCV co-infection were recruited from the Copenhagen comorbidity in HIV infection (COCOMO) study.
Sex and age matched uninfected controls were recruited from the Copenhagen General Population Study.

eGFR and study endpoints

In all participants *a single* blood sample was collected. Serum creatinine was used to calculate estimated glomerular filtration rate (eGFR) using the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) formula in accordance with European AIDS Clinical society (EACS) guidelines [4,5]

Reduced kidney function was defined as eGFR ≤60 mL/min/1.73m²

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Statistical analysis

We used logistic regression analyses to determine risk factors associated with reduced kidney function.
We adjusted for age, sex, BMI, cumulative smoking, diabetes and hypertension. We also assessed whether various HIV-related factors were each associated with reduced kidney function

Table 2

Variable	Odds Ratio (95%CI) for eGFR ≤60 ml/min/1.73m²	p-value
Age (OR: by 10 years)	5.4 (3.9-7.4)	<0.001
Sex, (OR: female vs. male)	5.0 (2.6-9.8)	<0.001
Ancestry, (OR: other Scandinavian vs Danish)	1.4 (0.5-3.7)	0.475
HIV (OR: yes vs. no)	3.4 (1.8-6.4)	<0.001
BMI (kg/m²) (OR: by 1 increase in BMI)	1.0 (0.95-1.1)	0.546
Pack years (OR: by 10 years)	0.89 (0.8-1.0)	0.105
Diabetes (OR: yes vs. no)	2.9 (1.2-6.7)	0.012
Hypertension (OR: yes vs. no)	0.9 (0.5-1.9)	0.851
Educational level (REF: No education)		0.454
— Short (<3 years)	0.6 (0.1-2.9)	
— Vocational	1.0 (0.3-3.4)	
— Middle length	0.8 (0.2-2.6)	
— University degree	1.3 (0.4-4.8)	

Adjusted for age, sex, HIV, BMI, pack years, diabetes and hypertension

Table 2. . Multivariable logistic regression analyses to determine whether HIV is independently associated with reduced kidney function.

Table 3

HIV-specific characteristics	PLWH (n=598)	Odds Ratio (95%CI) for eGFR <60 ml/min/1.73m²	p-value
Mode of transmission, n (%) (REF: MSM)	457 (77)	REF	0.189
— Heterosexual	110 (18)	2.0 (0.4-9.7)	
— Other	25 (4)	8.0 (1.2-51.4)	
Current CD4, median (IQR) (OR: by 100 pr. µl)	700 (521-900)	1.0 (0.8-1.2)	0.768
Current CD4, n (%) (REF: >500)	472 (79)	REF	0.238
— <200	15 (2.5)	NA	
— ≥200-350	33 (5.5)	7.9 (1.1-56.8)	
— ≥350-500	78 (13)	1.4 (0.3-6.9)	
CD4 nadir, n (%) (REF: <200)	245(41)	REF	0.637
— ≥200-350	218(37)	1.2 (0.2-7.6)	
— ≥350-500	77(13)	NA	
— >500	55(9)	13.7 (0.6-327.2)	
Time since HIV diagnosis, months, median (IQR), (OR: by 1 year)	169 (87-263)	1.1 (0.9-1.1)	0.669
History of AIDS, n (%), (OR: yes vs. no)	100 (17)	1.8 (0.5-6.7)	0.714

Abbreviations: MSM, men who have sex with men; AIDS, acquired immune deficiency syndrome; OR adjusted for age, sex, HIV, BMI, pack years, diabetes and hypertension

Table 3. HIV-related variables and multivariable logistic regression analyses of HIV-related variables to determine whether HIV is independently reduced kidney function

We additionally investigated whether HIV modifies the effect of age, hypertension and diabetes on reduced kidney function

RESULTS:

Clinical characteristics are presented in Table 1. Most PLWH were receiving cART (98.6%) and had suppressed viral replication (95.4%). Current median (IQR) CD4 count was 700 (521-900), few had CD4 count below 200 cells/mm³ (1.5%) but 41 % had a nadir CD4 count below 200 cells/mm³ (Table 3).

Among 598 PLWH and 2,598 controls, the prevalence of reduced kidney function was 4% [95%CI: 2%-5%] and 2% [95%CI: 1%-2%], respectively.

After adjustment, HIV status was independently associated with reduced kidney function, odds ratio (OR): 3.4 [95%CI: 1.8-6.3]. Aside from HIV, older age (OR per decade older: 5.3 [95%CI 3.9-7.2]), male sex (OR: 4.3 [95%CI 2.2-8.3]), and diabetes (OR: 2.9 [95%CI 1.2-6.7]) were independently associated with reduced kidney function

There was no interaction between diabetes and HIV status or between HIV status and hypertension.

We found evidence of interaction between age and HIV status on reduced kidney function in our adjusted model with accentuated effects of age among PLWH. Among PLWH, the odds ratio of reduced kidney function per decade older was 15.8 [95%CI: 5.6-44.7] and 4.6 [95%CI: 3.2 6.7] for uninfected controls (p for interaction = 0.016)

Mode of transmission, current CD4 level, CD4 level nadir, time with HIV and previous AIDS-defining diagnosis were not associated with reduced kidney function (table 3).

CONCLUSIONS

- Prevalence of reduced kidney function is higher in PLWH than in uninfected controls.

- HIV was independently associated with reduced kidney function and the effect of HIV seemed to be accentuated among older individuals.

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