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Prevalence and prognostic factors of chronic kidney disease in HIV-infected patients, HIV-NAT 006 cohort, Thailand

A. Avihingsanon[1,2], K. Praditpornsilpa [3], J. Wongsabut[1], A. Clark[1,4], , S.J. Kerr[1,4], S. Ubolyam[1], P. Phanuphak[1], J. Ananworanich [1,2,5], N. Hiransuthikul[6], K. Ruxrungtham[1,2] and HIV-NAT 006 study team

[1]HIV Netherlands Australia Thailand (HIV-NAT) Research Collaboration, Thai Red Cross AIDS Research Center Bangkok; [2]Immunology and Allergy Division, Department of Medicine, Faculty of Medicine, Chulalongkorn University, Thailand; [3] Renal Division, Department of Medicine, Faculty of Medicine, Chulalongkorn University, Thailand; [4]National Centre in HIV Epidemiology and Clinical Research, The University of New South Wales, Sydney, Australia; [5]South East Asia Research Collaboration with Hawaii, Bangkok, Thailand; [6] Preventive Medicine, Faculty of Medicine, Chulalongkorn University, Thailand.

Mailing Address:
Anchalee Avihingsanon, MD
HIV Netherlands Australia Thailand Research Collaboration (HIV-NAT), 104 Ratchadamri Rd., Pathumwan, Bangkok, Thailand 10330
Email: anchalee.a@hivnat.org
Tel: 662-652-3040 ext 107
Fax: 662-252-5779

HIV–NAT

Background

- Chronic kidney disease (CKD) is a major public health problem worldwide, resulting in increased risk of cardiovascular morbidity and mortality.[1]
- Untreated HIV disease can result in renal dysfunction, especially in those with high viral loads and low CD4 counts. This is particularly a problem in resource limited settings where treatment is initiated late at low CD4 counts. It is made worse by the effects of ageing, metabolic disturbances, the use of nephrotoxic antiretroviral medications, or those used to prevent or treat opportunistic infections.
- CKD and factors associated with its development in Asians living with HIV have not been well defined.
- This aim of this study was to assess the prevalence, incidence and risk factors for CKD in a cohort of patients from Bangkok, Thailand.

Methods

- We assessed the development of CKD in HIV-infected Thais from the HIV Netherlands Australia Thailand Research Collaboration (HIV-NAT) in Bangkok, Thailand
- Estimated Glomerular Filtration Rate (eGFR) was calculated using the simplified modification of diet in renal disease equation (MDRD) and CKD was staged according to accepted NIH/NIDDK Kidney Disease Outcomes Quality Initiative standards.[2]
- Patients were divided into 3 groups based on baseline eGFR; normal (>90 mL/min/1.73m^2 without hematuria/proteinuria), mild CKD (60-89 mL/min/1.73m2), and advanced CKD (<60 mL/min/1.73m^2 regardless of hematuria/proteinuria).
- Time to event methods were used to estimate the incidence of CKD for those with GFR > mL/min/1.73m^2 at baseline. The endpoint was defined as time for GFR to fall below 60 mL/min/1.73m^2.
- A multivariate model assessing factors associated with the development of CKD was developed using Cox proportional hazards regression and a forward-stepwise approach.

Results

- 1317 (45% female) patients were enrolled into the study; 40% had baseline CD4 <200 cells/µL. Patient characteristics are shown in Table 1
- Median age at start of entry to study was 35 (IQR 30 – 40) years
- Median time on ART was 8.1 (4.7 - 10.2) years, and 303 (23%) patients had been exposed to indinavir (IDV)
- Most recent median body weight was 57.6 (57-65) kg and most recent median CD4 was 522 (378-706) cells/µL, and 87% HIV RNA undetectable at most recent test
- Median baseline GFR was 88 (IQR 77-100), none had GFR < 60 ml/min/1.73m^2 prior to taking ARV.
- **Overall CKD prevalence was 69% (39% mild and 30% advanced CKD [GFR 30-59: 26%, 15-29: 2.8%, <15: 1%]).**
- The incidence of advanced CKD for the whole cohort and TDF user were 4.8 per 100 person-years and 5.5 per 100 person-years, respectively.
- 846 patients were taking tenofovir (TDF). 120 (14%) and 18 (2%) needed TDF dose reduction or discontinuation, respectively.
- In Figure 2, in multivariate analysis, advanced CKD was associated with age >50 years [Hazard ratio (HR) 2.1; 95%CI 1.5-3.0], IDV exposure (HR 3.1; 95%CI 2.5-3.8), Diabetes mellitus [DM] (HR1.8; 95%CI 1.3-2.4), and TDF exposure (HR1.6; 95%CI

Table 1. Characteristics of patients

Characteristics GFR (ml/min/1.73^2) n(%)	Total (n=1317)	Normal >90 (N=412), 31.3%	CKD stage I, II 60-89 (N=515), 39.1%	CKD stage III-V <60 (n=390), 29.6%	P*
Median (IQR) age, years	34.7 (30.2-40.0)	32.5 (28.3- 36.9)	34.7 (30.0-39.7)	37.2 (32.7- 43.5)	<0.01
n(%) female	598 (45.4)	189 (45.9)	258(50.1)	158 (38.7)	0.01
Median (IQR) weight (kg)	57.6(51-65.3)	57.1 (50 - 66)	57.6 (51.5- 65)	58 (51.9-66.7)	0.24
Median (IQR) current CD4 count (cells/µL)	539 (378 -706)	523 (366 – 680)	539 (395 – 710)	564.5 (400 – 715)	0.11
n(%) Nadir CD4 < 200 cells/µL	522 (39.6)	106 (25.7)	233 (45.2)	183 (46.9)	< 0.01
n(%) Patients with					
Current HIV-RNA < 50 copies/mL	1136 (86.6)	339 (82.3)	452 (87.8)	343 (88.0)	0.33
Median (IQR) baseline creatinine (mg/dl)	0.9 (0.8-1.07)	0.8 (0.7 - 0.9)	0.97 (0.83-1.1)	1.02 (0.87 - 1.19)	< 0.01
Median baseline (IQR) GFR (ml/min/1.73^2)	93 (81-105)	101 (95-111)	82 (76-88)	78 (66-91)	<0.01
n(%) Patients are currently taking TDF	846 (64.2)	277 (67.2)	362 (70.3)	207 (53.1)	<0.01
n(%) Patients are currently taking					
PI based HAART	928 (72.0)	283 (71.5)	348 (69.3)	292 (76.0)	0.08
NNRTI based HAART	359 (28.0)	113 (28.5)	154 (30.7)	92 (23.9)	
n(%) IDV exposure	303 (23.0)	67 (16.3)	55 (10.7)	181 (46.4)	<0.01
Median (IQR) accumulation of					
IDV exposure (years)	4.0 (1.6 - 4.2)	1.5 (0.5-3.9)	2.0 (1.0 - 3.3)	3.3 (2.3 - 4.3)	< 0.01
n(%) d4T exposure	742 (56.3)	225 (54.6)	300 (58.3)	217 (55.6)	0.38
n(%) Patients are currently taking ATV	178 (13.5)	56 (13.6)	48 (9.3)	65 (16.7)	0.02
Median (IQR) duration of					
ARV (years)	8.1 (4.7 - 10.2)	7.0 (3.7- 9.9)	6.9 (4.1 - 9.5)	9.9 (7.4 - 12.5)	<0.01
n(%) hepatitis B coinfection	129 (11.4)	43 (10.4)	56 (10.9)	30 (9.1)	0.29
n(%) hepatitis C co-infection	74 (6.7)	27 (6.6)	30 (5.8)	17 (5.3)	0.38
n(%) diabetes	87 (6.6)	18 (4.4)	20(3.9)	49 (12.6)	<0.01
n(%) hypertension	148 (11.2)	29 (7.0)	44 (8.5)	75 (19.2)	<0.01
n(%) ARV Naïve at baseline	998 (76.5)	332 (80.6)	429 (88.3)	237 (60.9)	<0.01
n(%) proteinuria	135 (10.3)	0	102 (19.8)	33 (8.5)	<0.01
n(%) hematuria	100 (7.6)	0	78 (15.1)	22 (5.6)	0.01
n(%) Metabolic syndrome	133 (10.1)	24 (5.8)	37 (7.2)	82 (21.0)	<0.01
n(%) Lipodystrophy	566 (17.4)	151 (36.7)	203 (39.4)	212 (54.4)	<0.01

* P value was analyzed by Kruskal Wallis test for continuous data and chi-square for categorical data

Figure 1. KM curve showing development of CKD by baseline eGFR

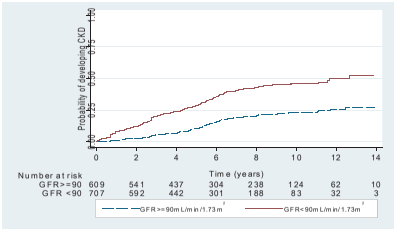
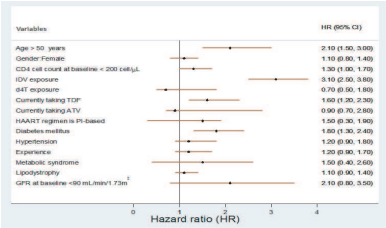


Figure 2. Results from multivariate analysis showing hazard ratios and 95% confidence intervals for risk of developing CKD.



Conclusions

There was a high prevalence of advanced CKD among HIV-infected Thais, particularly those with older age, DM and exposure to IDV or TDF. Close monitoring of renal function is warranted among Asian patients with these risk factors, especially when potentially nephrotoxic ARV are being used.

References

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