

Comparison between a UK versus Japanese HIV cohort

G P R Manmathan^{1,3}, R Ramphul², C Little³, T Kotecha³, A S Hunter¹, N Ngwu¹, N Hemat¹, T Barber¹, S Kinloch-de Loës¹, M A Johnson¹, F Burns^{1,4} and R D Rakhit³.

1) Department of HIV Medicine, Royal Free London NHS Foundation Trust, London, UK

2) Renal and Transplantation Unit, St George's University of London, UK

3) Institute of Cardiovascular Science, University College London; Department of Cardiology, Royal Free Hospital, London, UK

4) Institute for Global Health, University College London, UK

Background:

HIV-1 positive individuals face adverse consequences beyond HIV itself, including traditional risk factors for the development of chronic kidney disease (CKD) and additional nephrotoxic effects of antiretroviral therapy. Therefore, CKD remains an important comorbid condition in people living with HIV (PLWH) and an emerging concern among HIV-negative persons receiving pre-exposure prophylaxis¹.

Clinicians can use several monitoring tools such as routine measurements of proteinuria, estimated glomerular filtration rate (eGFR mL/min) or the KDIGO risk score (Kidney Disease: Improving Global Outcomes), to identify high-risk individuals who may require intervention to prevent non-HIV related adverse outcomes including cardiovascular morbidity and mortality².

Methods:

A retrospective analysis from a HIV outpatient clinic over a 20 month period (02.2017 – 09.2018). Urine protein creatinine ratio (uPCR) data was retrieved from the Royal Free Hospital's pathology laboratory database, along with demographic data and eGFR within 6 months of the uPCR result; eGFR was adjusted for the Afro-Caribbean population (x1.21). Patients were categorised according to the modified KDIGO 2012 classification, replacing urine albumin creatinine ratio (ACR) with protein creatinine ratio (PCR) (see Table 1.) Comparison was made with a Japanese HIV cohort who had performed similar analysis on a large number of patients.

Table 1. Grading of Proteinuria. Adapted from Table 7: Relationship among categories for albuminuria and proteinuria. KDIGO 2012 Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease

Measure	Normal to mildly increased (A1)	Moderately increased (A2)	Severely increased (A3)
ACR (mg/mmol)	< 3	3 – 30	> 30
PCR (mg/mmol)	< 15	15 - 50	> 50
Protein reagent strip	Negative to trace	Trace to +	+ or greater

Results:

8,400 uPCR tests were performed in 2,941 PLWH during this period; 94 patients were excluded due to urine contamination/leakage, or not having an eGFR or uPCR recorded within 6 months, leaving 2,847 PLWH with available data. Mean age was 49.7 years (SD ± 10.3), 24.9% were female, 56.7% White Caucasian and 29.6% were of Black African/Caribbean ethnicity.

Table 2. Distribution of CKD using uPCR.

PCR mg/mmol	Number	Percentage
Normal <15	2107	74.0%
Moderate 15-50	645	22.7%
Severe >50	95	3.3%
Total	2847	

Table 3. Distribution of CKD severity using eGFR.

CKD	eGFR	Number	Percentage
G1	>90	1299	45.6%
G2	60-89	1328	46.6%
G3a	45-59	170	6.0%
G3b	30-44	21	0.7%
G4	15-29	13	0.5%
G5	<15	16	0.6%
TOTAL		2847	

Conflicts of Interest:
None Declared

Table 4. Distribution of PLWH determined by the Modified KDIGO 2012 classification.

CKD Grading	eGFR	Proteinuria		
		A1	A2	A3
G1	>90	35.0%	9.8%	0.9%
G2	60-89	34.9%	10.6%	1.1%
G3a	45-59	3.8%	1.8%	0.5%
G3b	30-44	0.2%	0.3%	0.2%
G4	15-29	0.1%	0.1%	0.3%
G5	<15	0.0%	0.1%	0.5%

Table 5. CKD Prevalence using KDIGO classification. UK Population (n=2, 847) Vs Japanese (n=1,447) PLWH³.

Risk	Prevalence of CKD	
	UK	Japan
Low	69.9%	85.9%
Moderate	24.2%	11.0%
High	3.9%	2.1%
Very High	2.0%	1.0%

Discussion:

In a sub-group analysis there was no significant correlation between proteinuria and high blood pressure.

Using the Modified KDIGO 2012 classification we were able to identify a higher number of PLWH classified as at very high risk (from 1.1% to 2.0%). Furthermore when using proteinuria (A1) and eGFR (>60), 2,107 (74%) and 2,627 (91.2%) PLWH would be classified as low risk. However, when using KDIGO this would reduce to 1,991 (69.9%). Thus more people would require intervention and closer monitoring as 688 (24.2%) PLWH would become moderate risk compared to 645 (22.7%) using A2 or 170 (6%) using eGFR 45-59.

When compared to a Japanese cohort, where fewer people are undetectable, we have a higher CKD attrition rate in our HIV population. The Japanese authors analysed 1,447 PLWH, (97% males; 3% female) with an average age of 44.4 years. The higher prevalence of CKD between these populations may be due to ethnic variation, diet, a younger age, ART or a lower prevalence of other co-morbidities.

Conclusion:

Using the modified KDIGO 2012 classification we were able to identify more PLWH with moderate, high and very high CKD than through eGFR measurement alone.

We propose screening PLWH as soon as their CKD risk becomes moderate. Using the KDIGO classification and in particular ACR in stratification and treatment pathways to reduce morbidity and mortality.

References:

- Achhra AC, Nugent M, Mocroft A, Ryom L, Wyatt CM. Chronic Kidney Disease and Antiretroviral Therapy in HIV-Positive Individuals: Recent Developments. *Curr HIV/AIDS Rep.* 2016 Jun;13(3):149-57
- KDIGO 2012 Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease. *JAN 13 (3) 1.*
- Yanagisawa N, Muramatsu T, Yamamoto Y, Tsuchiya K, Nitta K, Ajisawa A, Fukutake K, Ando M. Classification of human immunodeficiency virus-infected patients with chronic kidney disease using a combination of proteinuria and estimated glomerular filtration rate. *Clin Exp Nephrol.* 2014 Aug;18(4):600-5