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## Introduction

- Acute kidney injury (AKI) in HIV-infected (HIV+) patients may be secondary to use of medications such as antihypertensives like diuretics, as well as antiretrovirals like tenofovir disoproxil fumarate (TDF).
- Studies linking TDF and AKI point out that patients use other nephrotoxic medications; however, none specifically mention diuretics.
- As HIV+ patients are living longer today and faced with comorbidities like hypertension, we postulated that using both diuretics and TDF would increase the risk for AKI.

## Aim

- To examine whether AKI in HIV+ patients on highly active antiretroviral therapy (HAART) is more common in those receiving a TDF-based regimen vs. those on a non-TDF-based regimen.
- To determine if the receipt of both TDF and a diuretic is associated with a higher risk for developing AKI among HIV+ patients on HAART with hypertension.

## Methods

- This was an observational study using data from the DC Cohort – a longitudinal research project collecting clinical data on HIV+ patients receiving care in 13 clinics across Washington, DC, since January 2011.
- Included adult (≥ 18 years old) HIV+ patients
  - Enrolled in the DC Cohort on or before 3/31/15.
  - On HAART for ≥ 14 days.
- Exclusion criteria:
  - Onset of AKI before the index date.
  - < two serum creatinine (SCr) levels on record.
  - Estimated glomerular filtration rate (GFR) < 15 ml/min/1.73m<sup>2</sup>.
- Observation period:
  - From index date (date enrolled in DC cohort) or 14 days after starting HAART, whichever came last, to the onset of AKI, death, loss to follow-up, discontinuation of HAART or diuretics, or 6/15/15.
- Exposure to diuretics was defined as a prescription for the diuretic medication ≥ 14 days.
- AKI was defined as a rise in SCr by ≥ 0.3mg/dL or a decrease in GFR by 50% within 3 months.
- If a drug was stopped, AKI was linked to that drug if it occurred within 28 days of stopping the drug.

## Methods

- We used descriptive and multivariate adjusted Cox proportional hazard analyses to examine correlates of AKI.

## Results

- Of 4681 patients, incidence of AKI → 6.14 cases per 100-person years (95% confidence interval 5.71-6.60).

### Demographics and Clinical Features of HIV+ Patients on HAART ≥ 14 Days Enrolled in the DC Cohort, 2011-2015

Characteristic	All Patients	On TDF	Not on TDF
<b>Total Patients Included, n</b>	4681	3884	797
<b>Gender, n (%)</b>			
Male	3405 (72.7)	2848 (73.3)	557 (69.9)
Female	1185 (25.3)	953 (24.5)	232 (29.1)
<b>Race/Ethnicity, n (%)</b>			
Non-Hispanic Black	3517 (75.1)	2905 (74.8)	612 (76.8)
Non-Hispanic White	718 (15.3)	600 (15.4)	118 (14.8)
Hispanic	202 (4.3)	178 (4.6)	24 (3.0)
<b>Age, n (%)</b>			
18-34 years	915 (19.5)	821 (21.1)	94 (11.8)
35-55 years	2627 (56.1)	2244 (57.8)	383 (48.1)
≥ 55 years	1139 (24.3)	819 (21.1)	320 (40.2)
<b>HIV Transmission, n (%)</b>			
MSM	1867 (39.9)	1622 (41.8)	245 (30.7)
High-risk Heterosexual	1382 (29.5)	1152 (29.7)	230 (28.9)
IVDU	308 (6.6)	237 (6.1)	71 (8.9)
Other	1124 (24.0)	873 (22.5)	251 (31.5)
<b>CD4 Count, n(%)</b>			
< 200 cells/mm <sup>3</sup>	491 (10.5)	419 (10.8)	72 (9.0)
200-349 cells/mm <sup>3</sup>	694 (14.8)	578 (14.9)	116 (14.6)
≥ 350 cells/mm <sup>3</sup>	3418 (73.0)	2822 (72.7)	596 (74.8)
Unknown	78 (1.7)	65 (1.7)	13 (1.6)
<b>Viral Load, n(%)</b>			
0-199 copies/mL	3681 (78.6)	3013 (77.6)	668 (83.8)
200-299 copies/mL	97 (2.1)	86 (2.2)	11 (1.4)
≥ 300 copies/mL	820 (17.5)	714 (18.4)	106 (13.3)
Unknown	83 (1.8)	71 (1.8)	12 (1.5)
<b>Baseline GFR, n (%)</b>			
≥ 90 mL/min/1.73m <sup>2</sup>	2472 (52.8)	2175 (56.0)	297 (37.3)
60-89 mL/min/1.73m <sup>2</sup>	1874 (40.0)	1551 (39.9)	323 (40.5)
30-59 mL/min/1.73m <sup>2</sup>	308 (6.6)	153 (3.9)	155 (19.4)
15-29 mL/min/1.73m <sup>2</sup>	27 (0.6)	5 (0.1)	22 (2.8)
<b>HBV at index date, n (%)</b>	160 (3.4)	146 (3.8)	14 (1.8)
<b>HCV at index date, n (%)</b>	601 (12.8)	458 (11.8)	143 (17.9)
<b>Diabetes at index date, n (%)</b>	487 (10.4)	355 (9.1)	132 (16.6)
<b>Hypertension at index date, n(%)</b>	1416 (30.2)	1073 (27.6)	343 (43.0)
<b>NSAIDs at index date, n (%)</b>	260 (5.6)	213 (5.5)	47 (5.9)
<b>Diuretics at index date, n (%)</b>	180 (3.8)	142 (3.7)	38 (4.8)
<b>AKI at follow-up, n (%)</b>	541 (11.6)	403 (10.4)	138 (17.3)

Key: n-total number of patients; IVDU-Intravenous drug use; MSM-men who has sex with men; GFR-Glomerular filtration rate; IQR-Interquartile range; HBV-Hepatitis B virus; HCV-Hepatitis C virus; AKI-Acute kidney injury.

## Results

### Hazard Ratios for Incident AKI among HIV+ Patients on HAART, DC Cohort, 2011 – 2015 (N = 4,681).

Characteristic	Univariable		Multivariable	
	HR (95% CI)	P-Value	HR (95% CI)	P-Value
Age (per 10 years)	1.6 (1.5, 1.7)	<0.001	1.2 (1.1, 1.3)	<0.001
Female at birth	0.6 (0.5, 0.8)	<0.001	0.6 (0.5, 0.8)	<0.001
Non-Hispanic Black	2.0 (1.6, 2.5)	<0.001	1.5 (1.1, 1.9)	0.003
<b>HIV Transmission</b>				
MSM	Referent		Referent	
High-risk heterosexual	1.6 (1.3, 2.0)	<0.001	1.2 (1.0, 1.6)	0.094
IVDU	4.5 (3.5, 5.7)	<0.001	1.7 (1.2, 2.3)	0.002
CD4 < 200 cells/mm <sup>3</sup>	2.2 (1.8, 2.7)	<0.001	1.7 (1.3, 2.2)	<0.001
Viral Load (log <sub>10</sub> copies/mL)	1.1 (1.1, 1.2)	<0.001	1.1 (1.1, 1.2)	<0.001
<b>Base GFR (ml/min/1.73m<sup>2</sup>)</b>				
≥90	Referent		Referent	
60-89	1.7 (1.4, 2.1)	<0.001	1.7 (1.4, 2.0)	<0.001
45-59	4.5 (3.4, 5.9)	<0.001	3.4 (2.5, 4.6)	<0.001
30-44	5.3 (3.4, 8.2)	<0.001	4.4 (2.7, 7.1)	<0.001
15-29	16.4 (9.9, 27.4)	<0.001	9.0 (5.1, 15.9)	<0.001
Hepatitis B Co-Infection	1.2 (0.8, 1.9)	0.31		
Hepatitis C Co-Infection	2.6 (2.2, 3.2)	<0.001	1.5 (1.2, 1.9)	<0.001
Diabetes	2.2 (1.7, 2.7)	<0.001	1.2 (0.9, 1.5)	0.12
Hypertension	1.8 (1.5, 2.1)	<0.001	1.2 (1.0, 1.4)	0.077
Use of NSAIDs	1.4 (1.0, 1.9)	0.047	1.2 (0.9, 1.7)	0.27
Exposure to TDF	0.6 (0.5, 0.8)	<0.001	1.0 (0.8, 1.2)	0.67

Key: n-total number of patients; AKI-Acute kidney injury; HR-Hazard ratio; CI-Confidence interval; GFR-Glomerular filtration rate; TDF-Tenofovir disoproxil fumarate; MSM-Men who have sex with men; IVDU-intravenous drug use

## Conclusion

- AKI was commonly seen in HIV+ adults across multiple clinics in Washington, DC from 2011 – 2015.
- TDF usage was not associated with AKI among HIV+ adults on HAART.
- Combination of diuretics and TDF therapy did not predispose patients to AKI, thereby suggesting that control of blood pressure may be more important than choice of anti-hypertensive medication in preventing AKI in HIV+ adults.

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## Results

### Hazard Ratios for Incident AKI among Hypertensive HIV+ Patients Receiving Concurrent HAART and Antihypertensive Medication, DC Cohort, 2011 – 2015 (N = 520).

Characteristic	Univariable		Multivariable	
	HR (95% CI)	P-Value	HR (95% CI)	P-Value
Age (per 10 years)	1.9 (1.5, 2.4)	<0.001	1.4 (1.0, 1.8)	0.030
Female at birth	0.4 (0.2, 0.8)	0.007	0.6 (0.3, 1.3)	0.18
Non-Hispanic Black	0.9 (0.5, 1.6)	0.70		
<b>HIV Transmission</b>				
MSM	Referent		Referent	
High-risk heterosexual	1.2 (0.7, 2.1)	0.49	1.2 (0.6, 2.2)	0.64
IVDU	2.1 (1.1, 4.0)	0.021	1.4 (0.6, 3.1)	0.44
CD4 < 200 cells/mm <sup>3</sup>	2.3 (1.1, 4.6)	0.023	2.4 (1.1, 5.3)	0.023
Viral Load (log <sub>10</sub> copies/mL)	1.1 (0.9, 1.3)	0.20		
<b>Base GFR (ml/min/1.73m<sup>2</sup>)</b>				
≥90	Referent		Referent	
60-89	2.0 (1.1, 3.6)	0.024	1.6 (0.9, 3.0)	0.14
45-59	5.5 (2.8, 10.9)	<0.001	3.7 (1.7, 8.3)	0.001
30-44	9.6 (3.5, 26.5)	<0.001	8 (2.6, 24.8)	<0.001
15-29	10.5 (2.4, 46.1)	0.002	5.2 (1, 26.1)	0.046
Hepatitis B Co-Infection	2.1 (0.8, 5.8)	0.14	2.0 (0.7, 5.7)	0.21
Hepatitis C Co-Infection	1.5 (0.9, 2.5)	0.10	1.3 (0.7, 2.6)	0.44
Diabetes	1.7 (1.1, 2.8)	0.029	1.2 (0.7, 2.0)	0.55
Use of NSAIDs	1.2 (0.7, 2.1)	0.44		
Exposure to diuretics	1.2 (0.6, 2.3)	0.59		
Exposure to TDF	0.6 (0.4, 1.0)	0.039	0.8 (0.5, 1.4)	0.45

Key: n-total number of patients; AKI-Acute kidney injury; HR-Hazard ratio; CI-Confidence interval; GFR-Glomerular filtration rate; TDF-Tenofovir disoproxil fumarate; MSM-Men who have sex with men; IVDU-intravenous drug use