Chronic Kidney Disease among HIV and HIV/HCV Co-infected Individuals in Washington, DC

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Abstract

Background: Hepatitis C (HCV) infection has been identified in 25–30% of HIV-infected persons in Western Europe and the United States. HCV is associated with increased risk for chronic kidney disease (CKD), both with and without HIV co-infection.
Methods: This is a retrospective cohort analysis of HIV-infected adults enrolled in the DC Cohort study at Georgetown University Hospital. Clinical and laboratory data were extracted from electronic medical records of consenting adults. Kidney function (eGFR) was estimated using the CKD-EPI formula. Descriptive statistics were derived using tests to determine differences by co-infection status. Multivariate logistic regression (MVR) was used to identify factors associated with reduced kidney function (SAS *v*9.4*)*.
Results: Among 771 HIV-infected patients enrolled between 2011-2014, the median age was 48 years, 73.4% were male, 50.3% Black, median enrollment CD4 546.5 cells/μL and HIV RNA <20 copies/mL, and 93 (12.1%) were HCV co-infected. There is a higher prevalence of CKD stages 2-5 (35.4 vs. 21.4%, p=0.0049) among co-infected individuals. Combination antiretroviral therapy regimens differed by HCV status with greater integrase strand transfer inhibitor (INSTI) usage with co-infection (44.1 vs. 24.6%, p=0.0002) and more Tenofovir disoproxil fumarate (TDF) (69.8 vs. 60.2%, p=0.0197) and non-nucleoside reverse transcriptase inhibitor (32.9 vs. 19.4%, p=0.0048) usage with HIV mono-infection. In MVR analysis, older age (OR 1.08 (95% CI: 1.06 – 1.11); p= <0.0001), Hepatitis B (2.45 (1.16 – 5.18); p= 0.0187), and current INSTI use (1.77 (1.12 – 2.80); p=0.0142) was significantly associated with reduced eGFR (<90 mL/min/1.73 m^2) but not current TDF use (0.41 (0.26 – 0.64); 0.0142).
Conclusions: We identified differential antiretroviral usage patterns with HIV/HCV co-infection. Higher INSTI use may be driven by efforts to minimize drug interactions with HCV medications. The non-deleterious effect of TDF was surprising given the inherent risk for kidney dysfunction conferred by TDF. Further studies are needed to determine the underlying pathophysiology of kidney dysfunction modulated by HIV infection and antiviral agents.

Introduction

- Current epidemiologic studies suggest ~ one in six persons in North America have chronic kidney disease (CKD) – decreased glomerular filtration rate (GFR) or albuminuria - which over time may lead to end-stage renal disease (ESRD) and the possible need for dialysis or kidney transplant.[1]
- CKD is associated with Hepatitis C (HCV) infection, both with and without HIV co-infection.[2] Proposed pathogenesis of CKD with HIV/HCV include:
  - immune complex glomerulonephritis
  - increased risk for diabetes[3]
  - concurrent co-morbidities such as hypertension
- African Americans have a four-fold greater incidence of end stage renal disease compared to whites and make up 22% of Americans with chronic HCV infection.[2,4]
- This study aims to evaluate factors that may contribute to CKD among HIV and HIV/HCV co-infected individuals

Methods

- Retrospective cohort analysis of HIV-infected adults enrolled in the Georgetown University, a clinical research sub-site of the DC Cohort study, a clinical cohort in the District of Columbia
- Clinical and laboratory data were extracted from electronic medical records of consenting adults enrolled from February 2011–December 2014
- Kidney function (eGFR) was estimated using the patient's lowest creatinine measurement and the CKD-EPI formula
- Wilcoxon-Mann-Whitney, Fisher's Exact, Chi-Square tests to determine differences by HIV and HIV/HCV status
- Multivariate logistic regression (MVR) models to identify factors associated with reduced kidney function (eGFR ≤89 mL/min/1.73 m^2)
- All statistical tests were conducted using SAS *v*9.4 (Cary, North Carolina).

References

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Results

Table 1 – Participant Characteristics by HCV status among DC Cohort participants

	HIV n = 678	HIV/HCV n = 93	Total n = 771	*P* value
Age, yrs, median (IQR)	47 (38, 54)	56 (48, 60)	48 (39, 55)	**<0.0001[a]**
Gender, n (%)				0.2707[b]
Male	495 (73.01)	71 (76.34)	566 (73.41)	
Female	181 (26.70)	21 (22.58)	202 (26.20)	
Transgender (MTF)	1 (0.15)	1 (1.08)	2 (0.26)	
Transgender (FTM)	1 (0.15)	0 (0.00)	1 (0.13)	
Ethnicity/race, n (%)				0.5477[c]
Non-Hispanic White	193 (28.47)	30 (32.26)	223 (28.92)	
Non-Hispanic Black	339 (50.00)	49 (52.69)	388 (50.32)	
Hispanic	11 (1.62)	0 (0.00)	11 (1.43)	
Other	32 (4.72)	3 (3.23)	35 (4.54)	
Unknown	103 (15.19)	11 (11.83)	114 (14.79)	
Nadir CD4+ T cells/mm^3, median (IQR)	258 (105, 424)	248 (99, 357)	252.5 (105.0, 411.0)	0.3937[a]
Enrollment CD4+ T cells/mm^3, median (IQR)	545.5 (344.0, 757.0)	551.5 (396.5, 748.0)	546.5 (355.0, 756.0)	0.5800[a]
Enrollment HIV RNA, copies/mL, median (IQR)	19 (19, 179)	19 (19, 44)	19 (19, 140)	0.3270[a]

Abbreviations: MTF, Male-to-Female; FTM, Female-to-Male; IQR, Interquartile range.
[a] Wilcoxon-Mann-Whitney test
[b] Fisher exact test
[c] Chi-square test

Table 2 – Antiretroviral Usage by HCV status among DC Cohort participants

	HIV n = 678	HIV/HCV n = 93	Total n = 771	*P* value
ART naïve, n (%)	21 (3.10)	0 (0.00)	21 (2.72)	0.0963[a]
Current ARV regimen, n (%)				
NRTI	613 (90.41)	86 (92.47)	699 (90.53)	0.7661[b]
TDF	473 (69.76)	56 (60.22)	529 (68.61)	**0.0197[b]**
NNRTI	223 (32.89)	18 (19.35)	241 (31.26)	**0.0048[b]**
PI	354 (52.21)	54 (58.06)	408 (52.92)	0.4484[b]
ATV	138 (20.35)	16 (17.20)	154 (19.97)	0.3958[b]
LPV/r	39 (5.75)	3 (3.23)	42 (5.45)	0.2873[b]
DRV	150 (22.12)	26 (27.96)	176 (22.83)	0.2750[b]
Integrase Inhibitors	167 (24.63)	41 (44.09)	208 (26.98)	**0.0002[b]**

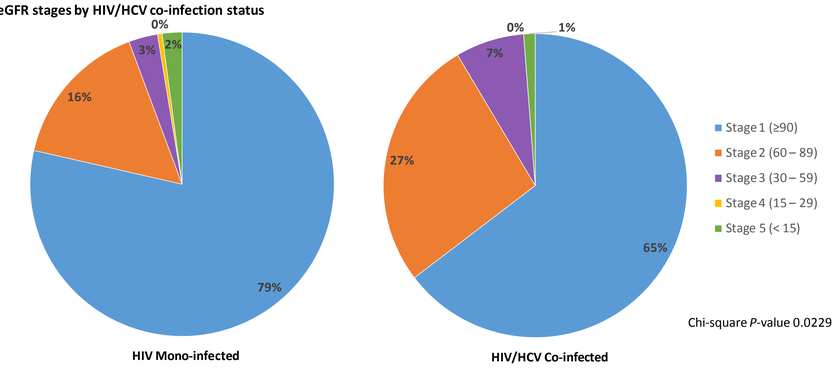
Abbreviations: ARV, Antiretroviral; NRTI, Nucleoside/Nucleotide Reverse Transcriptase Inhibitors; TDF, Tenofovir disoproxil fumarate; NNRTI, Non-Nucleoside Reverse Transcriptase Inhibitors; ATV, Atazanavir; LPV/r, Lopinavir/ritonavir; DRV, Darunavir; PI, Protease Inhibitors.
[a] Fisher exact test
[b] Chi-square test

Table 3 – Multivariable analyses of correlates associated with reduced kidney function (eGFR ≤89 mL/min/1.73 m^2) among DC Cohort participants by HCV infection status

	All participants OR (95% CI)[a]	*P*-value	Mono-infected participants OR (95% CI)[a,b]	*P*-value	Co-infected participants OR (95% CI)[a,c]	*P*-value
Age, years	**1.08 (1.06 – 1.11)**	**<0.0001**	**1.09 (1.07 – 1.12)**	**<0.0001**	1.06 (0.99 – 1.13)	0.0925
Ethnicity/race					--[d]	
Non-Hispanic White	Reference		Reference			
Non-Hispanic Black	1.34 (0.81 – 2.22)	0.2742	1.67 (0.95 – 2.95)	0.0742		
Hispanic	0.77 (0.08 – 7.68)	0.8285	1.05 (0.10 – 10.61)	0.9669		
Other	1.88 (0.62 – 5.66)	0.2627	2.50 (0.76 – 8.18)	0.1298		
Unknown	**3.68 (1.93 – 7.02)**	**<0.0001**	**4.38 (2.16 – 8.85)**	**<0.0001**		
Platelet count less than 150x 10^3/uL	--[d]		--[d]		**4.43 (1.17 – 16.81)**	**0.0287**
Co-morbidities						
Hypertension	0.74 (0.47 – 1.17)	0.1974	0.72 (0.44 – 1.18)	0.1882	--[d]	
Hepatitis B	**2.45 (1.16 – 5.18)**	**0.0187**	2.17 (0.92 – 2.08)	0.0755	--[d]	
Current ARV regimen component						
Tenofovir disoproxil fumarate	**0.41 (0.26 – 0.64)**	**<0.0001**	**0.53 (0.32 – 0.87)**	**0.0118**	**0.12 (0.03 – 0.40)**	**0.0006**
Protease inhibitor	1.35 (0.88 – 2.07)	0.1734	--[d]		--[d]	
Integrase inhibitor	**1.77 (1.12 – 2.80)**	**0.0142**	**1.87 (1.13 – 3.10)**	**0.0148**	--[d]	
Non-nucleoside reverse transcriptase inhibitors	--[d]		--[d]		3.63 (0.89 – 14.84)	0.0727

Abbreviations: OR, odds ratio; CI, confidence interval; ARV, Antiretroviral.
[a] Model includes all variables listed.
[b] Multivariate logistic regression modeling reduced kidney function among HIV mono-infected participants.
[c] Multivariate logistic regression modeling reduced kidney function among HIV/HCV co-infected participants.
[d] Variable removed from final model in backward step-wise elimination procedure.

Figure 1 – eGFR stages by HIV/HCV co-infection status



Results

- Prevalence of decreased kidney dysfunction is higher among HIV/HCV co-infected individuals as shown in Figure 1
- We found that HIV/HCV co-infected participants were older and had a statistically significant higher prevalence of kidney dysfunction (eGFR <89 mL/min/1.73 m^2) compared to HIV mono-infected individuals, with 35.4% vs 21.4% respectively
- HIV/HCV co-infected participants were less likely to be on an ARV regimen consisting of Tenofovir disoproxil fumarate (TDF) or Nuclesoide/Nucleotide Reverse Transcriptase Inhibitors (NNRTI) and had higher usage of Integrase Strand Transfer Inhibitors (INSTIs). (Table 2)
- Current TDF use was not associated with kidney dysfunction, though fewer HIV/HCV co-infected individuals were on a TDF containing regimen
- More individuals using INSTIs had evidence of kidney dysfunction, but this did not appear to be mediated by HCV status

Conclusions

- We identified differential antiretroviral usage among HIV and HIV/HCV co-infected individuals in this clinical cohort
- TDF remains a useful agent among HIV/HCV co-infected individuals who have not had evidence of early deleterious effect on kidney function at treatment initiation
- TDF's inverse association with reduced kidney function may be due to physician's refrained TDF use among patients with low kidney function
- Higher INSTI use may be driven by efforts to minimize drug interactions with HCV medications
- The association of INSTI use and lower eGFR determined by calculated creatinine clearance may be artifactual due to the co-formulation of some of these agents with cobicistat
- Measurements of kidney function that do not rely on measured serum creatinine may be necessary to accurately determine kidney function in this subset of patients
- Further studies are needed to determine the underlying pathophysiology of kidney dysfunction modulated by HIV, HIV/HCV co-infection, and antiviral agents

THE DC COHORT
Advancing HIV Care and Treatment in the District of Columbia