Markers of Macrophage Activation and Kidney Function in People With and Without HIV

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BACKGROUND

- People with HIV (PWH) still face a reduced life expectancy compared to people without HIV and age-related comorbidities are important contributors to their excess mortality.
- HIV infects and activates macrophages, which produce important mediators of inflammation that may drive age-related comorbidities.
- Soluble macrophage activation markers are higher in people with HIV (PWH), even among those who are virally suppressed, and are associated with prevalent and progressive subclinical cardiovascular disease and HIV-associated neurocognitive impairment.

Hypothesis: Markers of macrophage activation will be associated with lower kidney function among PWH.

METHODS

- We performed a cross-sectional study nested within 2 prospective U.S. multicenter cohorts of persons with and without HIV; the Women's Interagency HIV Study (WIHS) and the Multicenter AIDS Cohort Study (MACS).

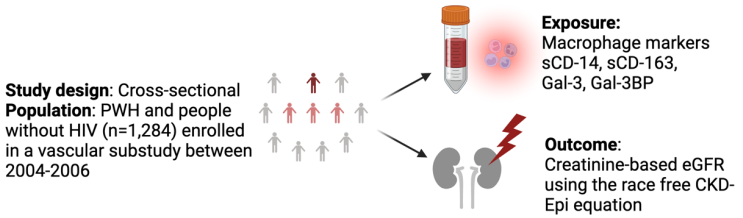


Figure 1. Study Design Overview

- Serum levels of macrophage markers soluble (s)CD-163, sCD-14, galectin-3 (Gal-3) and Gal-3 binding protein (Gal-3BP) were measured in 786 (73% PWH) women and 498 (65% PWH) men enrolled in a vascular substudy.
- Macrophage markers were log and Z-score transformed.
- Multivariable linear regression was used to determine the association between these markers and estimated glomerular filtration rate (eGFR). Interaction testing was performed to determine if these associations differed by HIV serostatus.

The macrophage markers galectin-3 and sCD-14 were associated with lower kidney function. These associations were more pronounced in PWH. These mediators of immune activation and inflammation may contribute to the development of kidney disease in PWH.

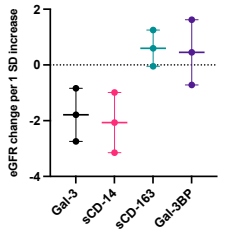
- Age was higher among men compared to women (median 49 vs 40 years) and women were more likely to be Black or Hispanic (p<0.05).
- More than two thirds of PWH were receiving antiretroviral therapy (ART), including ~30% that were receiving tenofovir disoproxil fumarate (TDF). A lower proportion of women with HIV were virally suppressed compared to men (45% vs 68%).

Table 1. Baseline Characteristics

	Women with HIV (n=570)	Women without HIV (n=216)	Men with HIV (n=332)	Men without HIV (n=166)
Age, years	40 (35, 46)	40 (34, 46)	48 (44, 53)	51 (46, 56)
Black race	305 (54%)	118 (55%)	108 (33%)	37 (22%)
Hispanic ethnicity	166 (29%)	53 (25%)	28 (8%)	15 (9%)
Hepatitis C infection	127 (22%)	33 (15%)	39 (12%)	6 (4%)
Hypertension	150 (26%)	56 (26%)	118 (36%)	67 (40%)
Diabetes	50 (9%)	24 (11%)	33 (10%)	12 (7%)
eGFR, mL/min/1.73m^2	95 (83, 111)	94 (80, 108)	93 (79, 105)	86 (77, 97)
CD4, cells/mm^3	450.5 (287, 654)	-	528.5 (370, 692)	-
HIV RNA undetectable	259 (45%)	-	227 (68%)	-
On ART	388 (68%)	-	268 (81%)	-
On TDF	156 (27%)	-	99 (30%)	-

Categorical variables represented as n (%), continuous variables represented as median (IQR)

RESULTS



- Gal-3 and sCD-14 were independently associated with lower eGFR (Figure 2).
- Each standard deviation (SD) increase in Gal-3 was associated with a -1.71 mL/min (95% CI -2.66, -0.84) lower eGFR.
- Each SD increase in sCD-14 was associated with a -2.07 mL/min (-3.15, -0.99) lower eGFR.

Figure 2. Association between Macrophage markers and eGFR among WIHS and MACS participants
*Adjusted for age, sex, race, ethnicity, education, diabetes, hypertension, hepatitis C, TDF

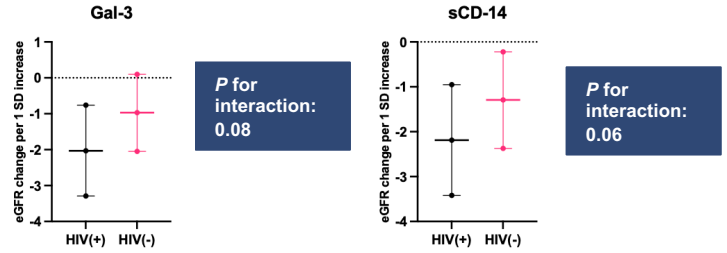


Figure 3. Association of Gal-3 and sCD-14 with eGFR by HIV serostatus
*Adjusted for age, sex, race, ethnicity, education, diabetes, hypertension, hepatitis C, TDF

CONCLUSIONS

- The macrophage markers Gal-3 and sCD-14 may have a role in subclinical kidney injury among PWH. Alternatively, kidney injury may increase levels of Gal-3 and sCD-14.
- Future work will examine the association between these macrophage markers and longitudinal kidney outcomes to identify whether they may play a causative role or have predictive value for kidney disease risk.

ADDITIONAL KEY INFORMATION

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Acknowledgements: Dr. Fisher's work is supported in part by the NIH/National Center for Advancing Translational Science (NCATS) Einstein-Montefiore CTSA Grant #UL1TR001073