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Association of HIV Infection and HIV/HCV Co-infection with C-reactive Protein Levels: The FRAM study

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Introduction

- Chronic infections such as HIV and HCV are associated with increased risks of cardiovascular disease
- Inflammation, as measured by CRP, is a predictor of atherosclerosis, but its role as a predictor in chronic infection is not understood
- Little is known about the relationship between HIV and CRP in the era of effective anti-retroviral therapy
- We evaluated the association between HIV infection and CRP and investigated the factors associated with CRP levels among HIV-infected persons in a nationally representative sample of HIV-infected subjects and in controls

Methods

- **Study design:** Multi-center cross sectional study
- **Study Population:** 1135 HIV-infected men and women enrolled in the Fat Redistribution and Metabolic Change in HIV Infection (FRAM) cohort
- **Control Population:** 281 controls studied in FRAM from the Coronary Artery Risk Development in Young Adults (CARDIA) cohort
- **Measurements:** CRP levels, HCV RNA level, MRI adipose tissue volume, gender, age, ethnicity, level of physical activity, current smoking status, current illicit drug use, alcohol intake, and HIV medical history
- **Statistics:** Mann-Whitney U and Fisher's exact test were used for comparison between the study and control group. Multivariable linear regression analysis was used to investigate the association of HIV infection with CRP levels after adjustment for potential confounding factors

Results

Table 1: Characteristics of HIV-infected and Control Subjects, stratified by gender

		Men		Women	
		HIV+	Control	HIV+	Control
n		799	150	336	131
Age (y)	Median (IQR)	43 (38-49)**	40 (37-43)	41 (36-47)	42 (37-44)
Race†	Caucasian	55%*	53%	33%*	50%
	African American	33%	47%	55%	50%
	Other	12%	0	12%	0
Physical Inactivity		48%**	25%	39%*	22%
No Alcohol use		25%*	16%	39%*	26%
Current Smoker		42%**	21%	45%**	13%
Current Crack/Cocaine		6%	4%	8%*	1%
BMI (kg/m²)	Median (IQR)	24 (22-27)**	27 (25-30)	26 (22-31)	28 (23-33)
VAT (L)	Median (IQR)	1.8 (0.8-3.0)	2.0 (1.1-3.0)	1.4 (0.6-2.4)*	1.1 (0.4-1.9)
Total SAT (L)	Median (IQR)	10 (7-14)**	15 (11-19)	26 (17-37)*	30 (20-40)
Menopausal		NA	NA	23%**	7%
Contraceptives		NA	NA	10%	15%
HRT		NA	NA	10%	5%
Hepatitis C		20%*	NA	26%	NA
Duration HIV (y)	Median (IQR)	8 (5-12)	NA	8 (6-11)	NA
Current CD4 (cells/uL)	Median (IQR)	345 (219-523)	NA	361 (196-557)	NA
HIV RNA (1000/mL)	Median (IQR)	0.4 (0.4-10.7)	NA	0.5 (0.4-14.8)	NA
Undetectable HIV/RNA		53%*	NA	46%	NA
Recent OI		2%	NA	4%	NA
AIDS by CD4/OI		73%	NA	73%	NA

NA=not applicable
†P-value for race testing difference in proportions between Caucasian and African-American.
**p<0.0001; *p<0.05

Results

- Because we identified a statistically significant HIV/HCV by gender interaction (p=0.002), we compared median CRP levels among controls, HIV- monoinfected, and HIV/HCV-co infected participants, stratified by sex

Table 2: Association of HIV and HIV/HCV-infection with CRP levels, stratified by gender

	HIV+/HCV- vs Control		HIV+/HCV+ vs Control	
	% Effect (95% CI)	P-value	%Effect (95% CI)	P-value
Men				
Unadjusted effect	75 (38, 116)	**<.0001**	10 (-25, 60)	0.64
Adjusted effect	88 (43, 143)	**<.0001**	4 (-35, 58)	0.90
Women				
Unadjusted effect	34 (-0.9, 84)	0.055	-43 (-62, -17)	**0.006**
Adjusted effect	5 (-27, 43)	0.80	-41 (-64, -11)	**0.012**

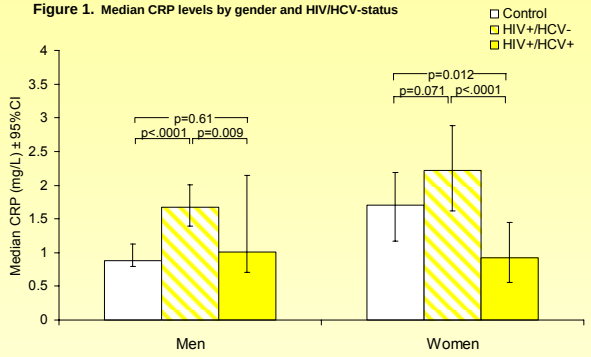
Participants were age restricted and those with recent opportunistic infections were excluded
Adjusted effects models control for HIV and HCV status, gender, age, ethnicity, lifestyle factors, visceral fat and subcutaneous fat.

Table 3. Characteristics associated with CRP among HIV-infected participants in FRAM

	% Effect (95% CI)	P-value
Demographic Factors		
Female vs Male	-19 (-36, 4)	0.097
African-American vs Caucasian	21 (-2, 50)	0.068
Hispanic vs Caucasian	21 (-8, 62)	0.18
Other vs Caucasian	-40 (-64, 3)	0.061
Age (per decade)	9 (-2, 21)	0.11
Adipose Tissue		
VAT (log 2)	17 (8, 26)	**<.0001**
Total SAT (log 2)	21 (7, 36)	**0.002**
Lifestyle		
Physical Activity: Inactive vs Active	31 (12, 56)	**0.002**
Non-Drinker vs Drinker	24 (3, 49)	**0.024**
Current Smoker vs non-smoker	33 (15, 59)	**<.0001**
Crack/Cocaine use	60 (10, 132)	**0.012**
HIV-related		
AIDS by CD4/OI	25 (2, 53)	**0.028**
Current HIV Viral Load (log 10)	5 (-5, 16)	0.35
Current CD4 (log 2)	-2 (-9, 7)	0.67
Hepatitis C (HCVRNA>615)	-50 (-59, -38)	**<.0001**

Also tested for inclusion in the model were MRI measurements of adipose tissue volume from other sites, other lifestyle factors, and HIV-related factors

Figure 1. Median CRP levels by gender and HIV/HCV-status



Participants were age restricted and those with recent opportunistic infections were excluded

Conclusions

- In the absence of HCV coinfection, HIV infection was associated with higher CRP levels in men with a similar trend for women
- However, adjusted levels of CRP were similar in HIV-monoinfected women and control women
- HCV coinfection was associated with lower CRP levels in both men and women, perhaps by suppressing production.
- Our data raise the question as to whether CRP will predict cardiovascular disease risk differently among patients with HCV or HIV/HCV coinfection.

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