



# Racial Comparison of D-dimer Levels in Adults Before and After HIV Infection

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## Abstract

**Background:** D-dimer levels predict mortality in persons with HIV infection, including those with viral suppression. Black race, older age, and comorbidities are associated with higher D-dimer levels in persons with and without HIV infection. Mechanisms leading to higher D-dimer related to HIV are poorly understood. We examined the effects of race and HIV by comparing changes in D-dimer levels among young adult African-Americans (AA) and Caucasians (C) before and after HIV infection.

**Methods:** We analyzed clinical and laboratory data for 207 participants in the US Military HIV Natural History Study, a cohort of US military personnel and beneficiaries living with HIV. Frozen stored sera were available at three time points (TP): TP1) pre-HIV seroconversion (SC), prior to last negative HIV test, TP2) >6 months post-HIV SC but prior to ART initiation, and TP3) >6 months post-ART with viral suppression on two successive evaluations. At each TP, we used a D-dimer assay validated for serum. No subject had known acute or chronic illness. Continuous variables were analyzed using Mann-Whitney U test and are expressed as median (IQR).

**Results:** Subjects included 94 AA and 113 C. 98% were male. AA were younger (median age [yrs] of 25 vs 28, p=0.02 at TP1; 30 vs 31, p=0.007 at TP2; and 31 vs 33, p=0.009 at TP3). Compared to C, AA D-dimer levels were similar at pre-HIV TP1 but were markedly higher at TP2 despite similar CD4 counts and HIV viral load (VL)(Table). AA and C did not differ in D-dimer levels at TP3, median time (mos) from estimated SC to ART initiation (24 [13, 47] vs 27 [16, 51], p=0.13), or time (mos) from ART to TP3 (11 [8, 14] vs 12 [10, 14], p=0.46).

	AA	C	p-value
D-Dimer (ug/ml)			
TP1	0.18 (0.08, 0.39)	0.16 (0.08, 0.29)	0.28
TP2	0.60 (0.29, 1.04)	0.36 (0.21, 0.84)	0.003
TP3	0.24 (0.16, 0.44)	0.24 (0.16, 0.39)	0.71
CD4 cells/ul			
TP2	339 (277, 449)	367 (294, 443)	0.62
TP3	549 (428, 778)	531 (435, 689)	0.55
Log10 HIV VL			
TP2	4.51 (3.95, 4.87)	4.54 (3.95, 4.97)	0.52
TP3	<1.70	<1.70	

**Conclusions:** Among young military members over the course from pre-HIV to post-ART, AA had a more pronounced rise in D-dimer post-SC but their pre-HIV and post-ART levels were similar to C. These data suggest racial differences in D-dimer may not be apparent in healthy young adults or persons with suppressed HIV and no comorbidities.

## Background

- D-dimer, a fibrin split product, is a marker for activation of the coagulation system
- D-dimer levels:
  - Are higher among HIV-infected compared with uninfected persons.<sup>1</sup>
  - Predict cardiovascular disease, thrombosis, and all-cause mortality in HIV and uninfected individuals.<sup>2-5</sup>
  - Increase with age, comorbidities, and poor functional status.<sup>6,7</sup>
  - Are higher among African-Americans<sup>7-9</sup>
  - Typically decrease with viremic suppression<sup>1</sup>
- Data on the effects of HIV and race on baseline D-dimer levels are lacking
- We compared D-dimer levels in young adult Caucasian and African-American military members:
  - Before and after HIV infection.
  - Before and after ART

## Methods

### Study population

- The U.S. Military HIV Natural History Study: An observational cohort evaluated at 6 Department of Defense medical treatment facilities in the U.S.

### Design:

- retrospective, observational

### Participant selection:

- Documented HIV seroconversion window <4 yrs
- Received ART for ≥6 months with HIV-1 RNA suppression on at least two successive measurements
- No hepatitis B or C, liver or cardiovascular disease, diabetes, malignancy, inflammatory conditions, or use of steroids prior to the post-ART time point
- Cryogenically stored serum was available at 3 time points:

**Pre-HIV** (time point 1, TP1) – the latest available sample at or prior to the last documented negative HIV test

**Pre-ART** (TP2) – the earliest available sample at least six months after estimated HIV seroconversion and three months after the first HIV positive test but before ART initiation

**Post-ART** (TP3) – the earliest available sample at least six months after ART initiation with viral suppression as above.

- HIV RNA Viral Load (VL) and CD4 cell count available at TP2 and TP3

### Race

- Self-reported as African-American or Caucasian (White, Non-Hispanic)

### D-dimer assay

- University of Vermont (Dr. Russell Tracy)
- Assay validated for serum samples

## Results

207 eligible participants:  
94 African-American, 113 Caucasian  
98% male

Results summarized in Table 1

### Key Findings:

D-dimer levels:

- Were similar by race pre-HIV
- Rose markedly higher in African-Americans pre-ART
- Decreased to similar levels in both races post-ART
- Did not return to pre-HIV levels
- No racial difference in CD4 counts, VL, time intervals

## Results

Table 1: Characteristics of Participants\*

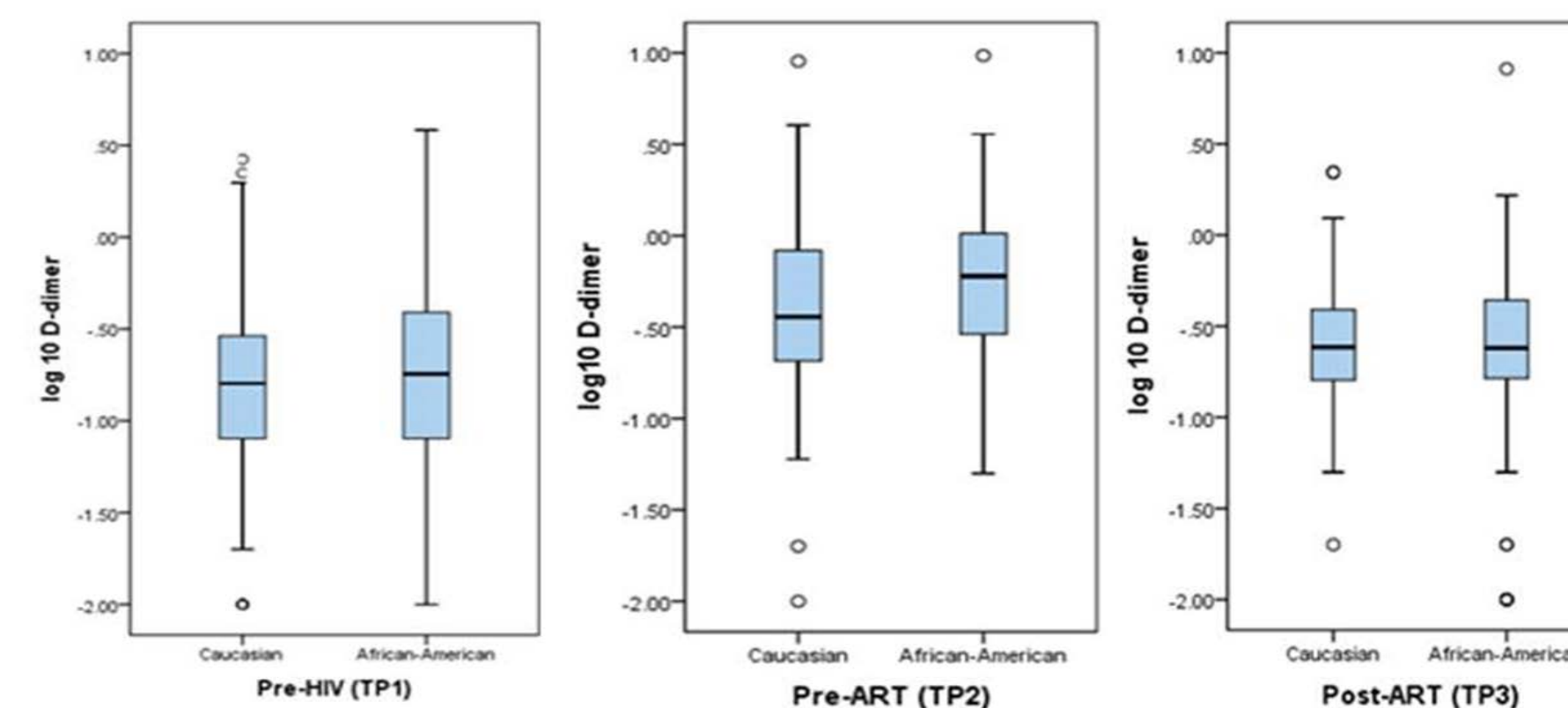
	African-American N=94	Caucasian N=113	p-value**
<b>Age (yrs)</b>			
Pre-HIV (TP1)	25 (22,31)	28 (24,34)	0.02
Post-HIV (TP2)	30 (24,34)	31 (28,37)	0.007
Post-ART (TP3)	31 (26,36)	33 (29,38)	0.009
<b>D-Dimer (ug/ml)</b>			
Pre-HIV (TP1)	0.18 (0.08, 0.39)	0.16 (0.08, 0.29)	0.28
Pre-ART (TP2)	0.60 (0.29, 1.04)	0.36 (0.21, 0.84)	<b>0.003</b>
Post-ART (TP3)	0.24 (0.16, 0.44)	0.24 (0.16, 0.39)	0.71
<b>CD4 cells/ul</b>			
Pre-ART (TP2)	339 (277, 449)	367 (294, 443)	0.62
Post-ART (TP3)	549 (428, 778)	531 (435, 689)	0.55
<b>Log10 HIV VL</b>			
Pre-ART (TP2)	4.51 (3.95, 4.87)	4.54 (3.95, 4.97)	0.52
Post-ART (TP3)	<1.70	<1.70	
<b>Time Interval (mos):</b>			
Seroconversion to ART***	24 (13, 47)	27 (16, 51)	0.13
ART Initiation to TP3	11 (8, 14)	12 (10, 14)	0.46

\*All values are expressed as Median (Interquartile Range)

\*\*Mann-Whitney U test

\*\*\*Seroconversion date estimated as the midpoint between positive and last negative HIV test

Figure 1: Box plot of log10 D-dimer levels by race at each time point



## Conclusions

- Rise in D-dimer was significantly more pronounced in African-Americans after HIV infection. Thus, blacks may be at higher risk of serious non-AIDS events with delay in ART.
- No racial difference in D-dimer levels were seen in young healthy military members prior to HIV infection. Higher levels in African-Americans observed in other studies may be related to age and comorbidities.
- D-dimer levels during viral suppression were similar in African-Americans and Caucasians. This suggests racial differences may be minimized by early treatment before comorbidities develop.
- D-dimer levels did not return to pre-HIV infection levels in either race. This is consistent with observations of D-dimer elevations in HIV viremically suppressed persons compared to uninfected populations.

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