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 levels in HIV poorly understood. We examined the effects of HIV and by changing comparing in-D-dimer levels among young adult African-Americans (AA) and Caucasians (Cauc) before and after HIV infection.

Methods: We analyzed clinical and laboratory data for 207 participants in the U.S. Military HIV Natural History Study, a cohort of 10 military personal and beneficiaries living with HIV. Cryogenically stored serum was available at 3 time points (TP1: pre-HIV seroconversion window, TP2: post-ART and TP3: negative HIV test at post-ART and prior to ART initiation). We compared D-dimer levels 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 disease.

Results: Subjects included 94 AA and 113 CA. 98% were male. AA were younger (median age [yrs] of 25 vs 22, p<0.001 at TP1, 23 vs 22, p<0.001 at TP2 and 23 vs 22, p<0.001 at TP3). Compared to CA, AA D-dimer levels were similar at pre-HIV TP1 and were markedly higher at TP3 despite similar CD4 counts and HIV viral load (1 x 10^6/mL). AA and CA did not differ in D-dimer levels at TP3, median (interquartile range) from nadir to ART initiation (24 [18, 40] vs 22 [16, 38], p=0.16). AA from TP1 (13 [8, 14] vs 12 [10, 14], p=0.46).

Conclusions: Among young military members over the course from pre-HIV to post-ART, the latest available time point – the earliest available sample at or prior to the last documented negative HIV test Post-Art (TP3) – 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 D-dimer, a fibrin split product, is a marker for activation of the coagulation system

Study population

- The U.S. Military HIV Natural History Study: An observational cohort evaluated at 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 suppression on at least two successive measurements

- No hepatitis B or C, liver cirrhosis or cancer

- No known acute or chronic disease

- No history of steroids prior to the post-ART time point

- Cryogenically stored serum was available at 3 time points:

  - Pre-HIV (TP1)
  - Post-ART (TP2)
  - Post-ART (TP3)

- Continuous variables were analyzed using Mann-Whitney U test and are expressed as median (interquartile range) 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 levels in HIV poorly understood. We examined the effects of HIV and by changing comparing in-D-dimer levels among young adult African-Americans (AA) and Caucasians (Cauc) before and after HIV infection.

- D-dimer levels:

  - post-ART, AA had a more pronounced rise in D-dimer post-SC but their pre-HIV and post-Art D-dimer levels were similar. These data suggest racial differences in D-dimer may not be apparent in healthy young adults or persons with suppressed HIV and no comorbidities.

- Results summarized in Table 1

- 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:

- Pre-HIV (TP1):

  - Similar by race pre-ART

  - Rose markedly higher in African-Americans pre-ART

  - Increased to similar levels in both races post-ART

  - Did not return to pre-HIV levels

  - No racial difference in CD4 counts, VL, time intervals

- Post-ART (TP2):

  - Negative HIV test

  - Markedly higher in AA than CA

  - Maximal difference seen at TP3

  - AA D-dimer levels decreased to similar levels in both races post-ART

- Post-Art (TP3):

  - The earliest available sample at least six months after ART initiation with viral suppression as above.

  - AA and CA D-dimer levels were similar at TP3, median (interquartile range) from nadir to ART initiation (24 [18, 40] vs 22 [16, 38], p=0.16). AA from TP1 (13 [8, 14] vs 12 [10, 14], p=0.46).

- Conclusions:

  - 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.

  - No hepatitis B or C, liver cirrhosis or cancer.

  - No history of steroids prior to the post-ART time point.

  - Cryogenically stored serum was available at 3 time points:

    - Pre-HIV (TP1)
    - Post-ART (TP2)
    - Post-ART (TP3)

  - Continuous variables were analyzed using Mann-Whitney U test and are expressed as median (interquartile range)