Psychosomatics 2016:57:423–430 Published by Elsevier Inc. on behalf of The Academy of Psychosomatic Medicine.

Original Research Reports

The Association Between Post-traumatic Stress Disorder and Markers of Inflammation and Immune Activation in HIV-Infected Individuals With Controlled Viremia

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Background: *Post-traumatic stress disorder (PTSD) may be associated with chronic immune dysregulation and a proinflammatory state. Among HIV-infected individuals, PTSD is associated with greater morbidity and mortality, but the association with immune dysfunction has not been evaluated. This study explores the association between PTSD and selected markers of inflammation and immune activation in a cohort of HIV-infected, virally-suppressed individuals.* **Methods:** *HIV-infected adults who were virologically controlled on antiretroviral medications were recruited through a screening protocol for studies of HIV-related neurocognitive disorders. Each participant underwent blood draws, urine toxicology screen, and completed the Client Diagnostic Questionnaire, a semistructured psychiatric interview.* **Results:** *Of 114 eligible volunteers, 72 (63%) were male, 77 (68%) African American, and 34 (30%) participants met criteria for PTSD. Participants with PTSD were more likely to be current smokers (79%) than those without (60%) ($p = 0.05$). The PTSD cohort had significantly higher total white blood cell counts (5318 and 6404 cells/uL, $p = 0.03$), absolute neutrophil count (2767 and 3577 cells/uL, $p = 0.02$), CD8% (43 and 48, $p = 0.05$), and memory CD8% (70 and 78%, $p = 0.04$); lower naïve CD8% (30 and 22%, $p = 0.04$) and higher rate of high-sensitivity C-reactive protein >3 mg/L (29 and 20, $p = 0.03$).* **Discussion:** *A high prevalence of PTSD was identified in this cohort of HIV-infected adults who were virally suppressed. These results suggest that PTSD may be associated with immune dysregulation even among antiretroviral therapy-adherent HIV-infected individuals.*

(Psychosomatics 2016; 57:423–430)

Key words: client diagnostic questionnaire, PLWH, immunophenotyping, antiretroviral therapy, post-traumatic stress, mental health.

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Published by Elsevier Inc. on behalf of The Academy of Psychosomatic Medicine.

BACKGROUND

Post-traumatic stress disorder (PTSD) is a highly prevalent comorbidity among adults with HIV infection, with the prevalence rates ranging from 23–42%.[1–3] Such high prevalence stands in sharp contrast to the 9.7% prevalence of PTSD in the general US population reported in large epidemiologic surveys,[4,5] but is less surprising considering that more than half of HIV-infected individuals report experiencing at least 1 severe traumatic event in their lifetime.[1,2]

Evidence suggests that PTSD and, to a smaller extent, a history of psychologic trauma without PTSD, may be associated with alterations in immune responsiveness and a proinflammatory state. Psychologic trauma survivors tend to have significantly lower percentages of naïve $CD8^+$ T cells, increased proportions of $CD3^+$ central and effector memory T cells, and a major reduction in the proportion of regulatory T cells when compared with nontraumatized individuals.[6,7] This effect is relatively more pronounced among trauma survivors with current PTSD than among trauma survivors without current PTSD,[6,7] and the severity of PTSD symptoms correlates with the degree of T-cell activation.[6] *In vitro* experiments with peripheral blood mononuclear cells harvested from trauma survivors either with or without current PTSD, and controls without trauma or PTSD, demonstrated decreased leukocyte glucocorticoid receptor density in both groups of trauma survivors and decreased dexamethasone-induced inhibition of T-cell proliferation only from individuals with current PTSD, suggesting that PTSD may be associated with a qualitatively different effect on immune regulation compared to trauma exposure alone.[8] In a prospective life-course study, a history of childhood maltreatment was predictive of serum high-sensitivity C-reactive protein (hsCRP) levels >3 mg/mL (a marker of a proinflammatory state and increased cardiovascular disease risk) 20 years later, even after controlling for key health behaviors, including smoking.[9] These reported associations of PTSD and trauma history with compromised immune responsiveness and proinflammatory state may explain why individuals suffering from PTSD are more likely to have infections, autoimmune disorders, and other inflammatory diseases than those without PTSD.[6,7]

To date, the effect of PTSD on circulating markers of immune activation or inflammation has not been evaluated in HIV-infected individuals. Growing evidence suggests that even a history of psychologic trauma alone is independently associated with a number of unfavorable clinical and behavioral outcomes among HIV-infected individuals. This includes increased AIDS-related mortality, opportunistic infections,[10] increased HIV viral load, as well as antiretroviral therapy (ART) nonadherence and unprotected sex, even after controlling for psychosocial factors and comorbidities (i.e., coping style, self-efficacy, social support, trust in the medical system, recent stressors, mental health, and substance abuse).[11] Given the high prevalence of PTSD among HIV-infected individuals, and the importance of immune regulation to HIV disease outcomes, it is important to know if the reported associations between PTSD and alterations in T-cell compartments and inflammation also exist among HIV-infected individuals with comorbid PTSD.

The hypothetical effect of PTSD on immune and inflammatory markers might be caused by the neuroendocrine or neuroimmune mechanisms suggested by the studies described earlier.[6–8] Alternatively, given the reported associations between psychologic trauma and ART nonadherence among HIV-infected individuals,[11] this effect may be caused by or mediated through ART nonadherence. This project is a cross-sectional exploratory analysis of selected immune and inflammatory biomarkers in a cohort of HIV-infected adults screened for both trauma and PTSD. To minimize the potential confounding effect of ART nonadherence on the association between PTSD and the biomarkers, this analysis was restricted to virally-suppressed HIV-infected individuals.

METHODS

Study Sample and Procedures

Participants were recruited through a natural history screening study of HIV-associated neurocognitive disorders. The objective of the natural history study is to determine the eligibility of HIV-infected individuals for participation in other Neuro-HIV studies at the NIH Clinical Center. The Institutional Review Board of the National Institute of Allergy and Infectious Diseases approved the study. Written informed consent was obtained from all participants.