Title

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Journal

AIDS and Behavior, 21(11)

ISSN

1090-7165

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Publication Date

2017-11-01

DOI

10.1007/s10461-017-1788-4

Peer reviewed

HHS Public Access

Author manuscript

AIDS Behav. Author manuscript; available in PMC 2018 November 01.

Published in final edited form as:

AIDS Behav. 2017 November ; 21(11): 3238–3246. doi:10.1007/s10461-017-1788-4.

Depression and anxiety are common in acute HIV infection and associate with plasma immune activation

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Abstract

This observational study of 123 Thai participants sought to determine the rate and severity of affective symptoms during acute HIV infection (AHI) and possible associations to disease mechanisms. At diagnosis, just prior to starting combination antiretroviral therapy (cART), AHI participants completed assessments of depression and anxiety symptoms that were repeated at 4, 12, and 24 weeks. Blood markers of HIV infection and immune activation were measured at study entry, with optional cerebrospinal fluid (CSF) measures. A high frequency of participants reported symptoms that exceeded published thresholds supportive of depression (55.0%) and anxiety (65.8%) at diagnosis, with significant reductions after starting cART. Meeting a threshold for clinically relevant depressive symptoms at study entry was associated with higher baseline plasma

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Compliance with Ethical Standards

Conflict of Interest: Author Joanna Hellmuth declares that she has no conflict of interest. Author Donn Colby declares that he has no conflict of interest. Author Victor Valcour has served as a consultant for ViiV Healthcare on topics unrelated to the work presented here. Author Duanghathai Suttichom declares that she has no conflict of interest. Author Serena Spudich declares that she has no conflict of interest. Author Jintanat Ananworanich has received honorarium from ViiV Healthcare, Merck and Roche for her participation in advisory meetings. Author Peeriya Prueksakaew declares that she has no conflict of interest. Author Napapon Sailasuta declares that she has no conflict of interest. Author Isabel Allen declares that she has no conflict of interest. Author Linda L. Jagodzinski declares that she has no conflict of interest. Author Bonnie Slike declares that she has no conflict of interest. Author Derek Ochi declares that he has no conflict of interest. Author Robert Paul declares that he has no conflict of interest.

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Ethical approval: All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

HIV RNA (5.98 vs. 5.50, t=2.46, p=0.015), lower CD4 counts (328 vs. 436 cells/mm_3, t=3.46, p=0.001), and higher plasma neopterin, a marker of macrophage activation (2694 vs. 1730 pg/mL, Mann-Whitney $U = 152.5$, p=0.011). Controlling for plasma HIV RNA and CD4 count, higher baseline plasma neopterin correlated with worse initial depression and anxiety scores. Depression and anxiety symptoms are frequent in acute HIV infection, associate with plasma immune activation, and can improve concurrent with cART.

Keywords

Acute infection; Depression; Anxiety; Neopterin; Men who have sex with men

INTRODUCTION

Depression is twice as frequent in people living with HIV compared to the general population [1] and is linked to worse disease outcomes, including reduced life expectancy [2, 3, 4]. In chronic HIV infection, reported rates of clinically relevant depression range from 7% to 42%, with anxiety ranging from 13% to 53% [5, 6, 7, 8, 9, 10, 11]. In a study of recently infected individuals, some of whom had been infected for only a few weeks (i.e., acute HIV infection) over 20% reported suicidal ideation in the preceding month [12]. Rates of post-traumatic stress disorder (PTSD) due to HIV diagnosis are as high as 30% [13]. Depression in early HIV infection is reported to occur in up to 48% of individuals [12, 14, 15], with anxiety in as many as 51% [16].

The broad published range in frequency of depression and anxiety in HIV is likely influenced by the different methods to capture affective symptoms, the approach of identifying any symptoms versus symptom severity that meets clinical thresholds, and participant heterogeneity across studies, including comorbidities known to increase the risk of affective disturbance. Indeed, the presence of depression in HIV is influenced by individual factors such as female sex [17, 18, 3], previous psychiatric history [19], and history of substance use [20]. Further, social factors, such as limited psychosocial support [21] and lower socioeconomic status [22] are associated with increased risk for depression in chronic HIV. In addition to the complex array of individual and psychosocial factors, biological aspects of HIV infection could influence the presence and severity of affective symptoms. There is increasing recognition that chronic viral infections like HIV have neuropsychiatric consequences [23], as the altered immune system in HIV may influence how the CNS regulates psychological states. HIV enters the central nervous system (CNS) within days of infection and is associated with early intrathecal immune activation [24, 25]. Evidence of neuronal damage is detectable within the first year of infection [26]. Studies report worsening depression associated with disease-related factors such as antiretroviral therapies [27] and the stage of HIV infection [21].

Existing studies are mixed concerning the relationships between biological aspects of HIV infection and affective disorders or symptoms. Some describe an inverse correlation between depressive symptoms and blood CD4 count [28] and a positive correlation between depressive disorders and plasma HIV RNA [29]. The direction of these associations is

consistent with other studies reporting a more rapid rate of CD4 decline with higher depressive symptoms [30], even when controlling for clinical and socioeconomic factors [3]. Similarly, others report elevated symptoms of depression and a decline in CD8+T cell counts and CD16+ natural killer cell counts [31]. However, another study has shown increased CD8+ T lymphocyte counts associating with symptoms of depression and anxiety [29]. By contrast, elevated symptoms of anxiety were associated with a higher CD4 count in one study [32], while others reported no associations between severity of self-reported affective symptoms or disorders and CD4 count [22, 33, 34]. The considerable individual, psychosocial, and disease-related heterogeneity of participants may add to the mixed findings in these studies.

Investigations focused on the expression of affective symptoms during acute HIV will help assess how these disorders evolve over time and after initiation of combination antiretroviral therapy (cART), and whether baseline symptoms persist despite HIV treatment. The present study assessed depression and anxiety symptoms in a homogeneous group of HIV treatment-naïve Thai participants during AHI immediately following diagnosis and after weeks 4, 12, and 24 weeks of cART. We investigated associations of affective symptoms with blood and CSF biomarkers of HIV infection and immunologic response prior to initiating cART.

METHODS

Participants

We included individuals diagnosed with acute HIV infection (AHI) from the previously described SEARCH 010/RV254 cohort in Bangkok, Thailand [35]. Study participants sought elective HIV testing at the Thai Red Cross Anonymous HIV clinic or were men who have sex with men (MSM) enrolled in a study at the Silom Community Clinic, both in Bangkok. Of the 108,099 samples screened for study inclusion between May 14, 2009 and July 31, 2014, we identified 228 cases of AHI using hierarchical algorithms from pooled nucleic acid and sequential EIA testing. The inclusion criteria were confirmed AHI in Fiebig I-V stage [36] and age ≥18 years. Exclusion criteria were a positive urine pregnancy test or the presence of known major medical or psychiatric disorders (e.g. schizophrenia, bipolar disorder). Informed consent was obtained from all individual participants included in the study. No participant entered the study on psychiatric medications. Of the 228 eligible participants, 189 elected to enroll. Eight additional participants were included through the Early Capture HIV Cohort (ECHO) Center in Pattaya, Thailand where individuals at high risk for HIV infection are screened for HIV every three days and are similarly identified in Fiebig stage IV AHI [37]. Of the 197 participants enrolled in the parent study, we excluded from this analysis one subject who dropped out, two who elected for delayed initiation of cART, and 71 who had incomplete demographic data (n=2) or psychiatric assessments (n=69).

Clinical and laboratory characterization

Infection duration for each participant was estimated based on self-report of a single exposure date or for those with multiple potential exposures, as the median of the dates. At study entry, we determined preceding or current symptoms of acute retroviral syndrome

(ARS) occurring after estimated infection date, using a standardized checklist of possible symptoms (adenopathy, anorexia, arthralgias, diarrhea, fatigue, fever, genital ulcers, headache, myalgias, nausea and emesis, neurologic symptoms, odynophagia, oral candidiasis, oral ulcers, pharyngitis, vaginal candidiasis, or weight loss). ARS was defined as the presence of ≥3 symptoms from estimated infection to study entry. Information regarding participant illicit drug use was obtained through structured interviews at study entry reflecting any self-reported use within the four months preceding enrollment. Information was obtained on the route, frequency, and class of substances used. After baseline study evaluations were complete, participants immediately started one of two cART regimens: efavirenz, tenofovir, and either emtricitabine or lamivudine (cART, 52%, n= 64) or the same cART regimen augmented with maraviroc and raltegravir (cART+, 48%, n=59) with a few substitutions as needed for side effects or resistance as previously described [38]. Expedited study evaluations were typically completed within 48 hours of diagnosis, and 96% of participants started cART within three days of study entry (range: 0–5 days; median: 0 days). Blood biomarkers of HIV infection were obtained at study entry, including HIV RNA, CD4 count, and neopterin, a marker of macrophage activation. A subset of participants underwent optional lumbar puncture at study entry (22%, n= 27) to measure cerebrospinal fluid (CSF) HIV RNA and neopterin. The lower limit of assay detection for CSF HIV RNA was 100 copies/mL. Lumbar puncture (LP) was only performed after obtaining depression and anxiety symptom assessments. Limited sample numbers for immune activation markers is due to less than 100% consent for LP for CSF, and not all collected samples were able to be processed for all immune activation markers. Single-voxel brain MRS was obtained at entry (35%, n=43) on a 1.5 Telsa GE Sigma HDx scanner, as previously described [39]. Metabolite ratios reflecting neuronal integrity (NAA/creatine), and inflammation (myoinositol/creatine; choline/creatinine) were examined in the basal ganglia, frontal gray matter, and frontal white matter regions.

Anxiety and Depression symptom measures

At baseline and weeks 4, 12, and 24 participants completed the English or a validated Thai version of the Hospital Anxiety and Depression Scale (HADS), a 14-item survey of current symptoms resulting in anxiety (HADS-A) and depression (HADS-D) sub-scores, with possible sub-scores ranging from 0–21 [10, 40]. The HADS was designed to avoid somatic components of affective symptoms, which commonly overlap with other medical conditions [41, 42]. Participants also completed the Thai or English version of the Patient Health Questionnaire-9 (PHQ-9), a nine-item survey assessing the frequency of depressive symptoms in the previous two weeks that has been validated in a Thai population [43]. The PHQ-9 has been found to have a sensitivity of 0.84, specificity of 0.77, and a negative predictive value of 0.99 using a threshold score ≥9 [42]. The PHQ-9 includes somatic symptoms and is derived from DSM-IV criteria for depression, with possible scores ranging from 0–27 [44]. The PHQ-9 is superior for detecting depression compared to the HADS and the WHO Well-Being Index 5 based on ICD-10 diagnostic criteria [42, 45]. Based on published thresholds, the presence of clinically relevant depressive symptoms was defined either as a score ≥10/27 on PHQ-9 (moderate depression) or ≥8/21 on HADS-D (borderline abnormal or abnormal depression), and the presence of clinically relevant anxiety symptoms was defied as ≥8/21 on HADS-A (borderline abnormal or abnormal anxiety) [44, 46].

Cronbach's alpha between the HADS-D and PHQ-9 in this sample is 0.781. At baseline, participants' self-reported level of distress was assessed with the Distress Thermometer [47]. These measures of psychiatric symptoms were obtained prior to other testing, including lumbar puncture, to minimize the influence of procedures on these assessments.

Statistical analyses

Descriptive statistics were calculated for all variables, with means and standard deviations calculated for continuous variables, and frequencies and percentages for categorical variables. Continuous data were examined to confirm compliance with assumptions of normality. Pearson's correlations were employed for parametric data, and Spearman's correlations for nonparametric data. Bivariate relationships were examined between disease biomarkers and depression and anxiety scores, and comparisons between groups were performed using two-tailed unpaired t-tests for continuous data, and Mann-Whitney *U* tests for ordinal data. Linear regressions were performed to assess the relationship between baseline plasma HIV RNA, CD4 count, plasma neopterin levels, and baseline depression and anxiety scores. Analyses were performed on Prism 6 (GraphPad Software) and Stata 13.1 (StataCorp, College Station, TX) and used $p \leq 0.05$ for statistical significance.

RESULTS

We identified 123 participants with AHI who had psychiatric data at study entry and weeks 4, 12, and 24 following cART. There was no attrition in the reported study. Compared to study participants, the excluded individuals (n=74) were similar in age, sex, percent of individuals defining risk as MSM, years of education, estimated infection duration, and Fiebig stage (all p-values > 0.05). Men comprised 94% of participants, with 97% of these self-identifying as MSM. Three participants identified as transgender women.

There were no group differences between participants with or without clinically relevant anxiety or depression symptoms either at baseline or at any point in the study in terms of age, sex, sexual orientation, years of education, estimated infection duration prior to study entry, drug use, Fiebig stage, or cART regimen (Table I). There was a trend towards participants in Fiebig stage III-V to meet thresholds for clinically relevant depressive symptoms at study entry compared to participants in Fiebig I/II (58% vs. 42%, $X^2=3.52$, p=0.061); however, this marginal significance was lost in models adjusting for plasma HIV RNA (p=0.392). Participants with clinically relevant depressive symptoms on the PHQ-9, which includes somatic symptoms, were more likely to have ARS compared to those not meeting these depression criteria (n= 44/45 vs. 47/58, $\chi^2=6.90$, p=0.009). The number (6.68 vs. 4.07, t=4.23, p<0.001) and average severity (7.47 vs. 4.86, t=3.18, p=0.002) of ARS symptoms were overall greater among those with clinically relevant depressive symptoms on the PHQ-9 compared to those who did not meet that threshold. These associations were not evident among those with clinically relevant depressive symptoms at baseline on the HADS-D depression or clinically relevant anxiety symptoms on HADS-A. We found a strong correlation between baseline HADS-D and PHQ-9 total scores (r=0.662, p<0.001). Baseline scores on the Distress Thermometer had positive correlations with baseline HADS-A

anxiety scores (r=0.669, p<0.001), HADS-D depression scores (r=0.627, p<0.001) and the PHQ-9 depression scores (r=0.629, p<0.001).

At study entry, 65.8% of participants met criteria for clinically relevant anxiety symptoms on the HADS-A (Fig. 1). Similarly, 45.5% of participants met the threshold for clinically significant depressive symptoms at baseline on the PHQ-9, with 40.6% on the HADS-D, and 55.0% met criteria on at least one depression measure. The occurrence of affective symptoms decreased significantly from study entry to week 4 for all measures (HADS-A; 65.8% to 24.4%, X^2=42.70, p<0.001; HADS-D: 40.6% to 17.1%, X^2=16.65, p<0.001; PHQ-9: 45.5% to 30.1%, X^2=6.24, p=0.012). From week 4 to 12, continued declines were seen in rates of clinically relevant depressive symptoms (HADS-D: 17.2% to 6.5%, X^2=6.61, p=0.010; PHQ-9: 30.1% to 17.1%, X^2=5.58, p=0.016), but not in rates of clinically relevant anxiety symptoms (HADS-A: 24.4% to 20.3%, X^2=0.59, p=0.444). There were no significant changes in frequency of clinically relevant anxiety or depression symptoms between weeks 12 and 24. At 24 weeks, 17.1% of participants still met criteria for anxiety on the HADS-A, 8.1% of participants met criteria for depression on the HADS-D, and 17.9% met criteria for depression on the PHQ-9. In the first six months following diagnosis, only three participants started medication for depression or anxiety, and none were started on selective serotonin reuptake inhibitors. Two participants were prescribed a low dose of alprazolam, which was needed for less than two months.

Participants experiencing clinically relevant depressive symptoms at study entry on at least one measure had higher average $\log_{10}$ plasma HIV RNA compared to those who did not (5.98 vs. 5.50, t=2.46, p=0.015, n=123, r=0.22) (Fig. 2A). Similarly, a lower mean CD4+ count was observed at baseline among participants with clinically relevant depressive symptoms at baseline on at least one measure (328 vs. 436 cells/mm^3, t=3.46, p<0.001, n=123, r=0.30) (Fig. 2B). Higher mean plasma neopterin (2694 vs. 1730 pg/mL, Mann-Whitney U=152.5, p=0.011, n=47) was observed in those with clinically relevant depressive symptoms at study entry (Fig. 2C) on either measure. Baseline CSF HIV RNA and CSF neopterin did not differ when examined by baseline depressive symptoms status on at least one measure; however, participants who met endorsed depressive symptoms of sufficient severity to meet the clinical threshold on the HADS-D had higher mean CSF neopterin compared to those that did not (3401 vs. 1140 pg/mL, Mann-Whitney U=18, p=0.028, n=19) (Fig. 2D). The presence or absence of clinically relevant anxiety symptoms at study entry was not associated with any of the examined plasma or CSF markers of HIV infection or immune activation.

Examination of symptom burden using a continuous scale revealed a modest correlation between the score on the PHQ-9 at baseline and plasma neopterin levels (r=0.29; p=0.045, n=42) (Fig. 3). Additionally, a modest inverse relationship was observed between CD4 count and baseline HADS-D (r=−0.24, p=0.012, n=123), PHQ-9 (r=−0.19, p=0.026, n=123) and HADS-A (r=−0.18, p=0.037, n=123). To examine the influences of HIV factors on affective scores at baseline, we employed cross-sectional linear regressions using covariates of baseline plasma HIV RNA, CD4 count, and plasma neopterin with total score on the HADS-A, HADS-D and PHQ-9. For all psychiatric measures, only baseline plasma neopterin correlated with baseline affective scores (HADS-A: t=5.09, p<0.001; HADS-D: t=5.65,

p<0.001; PHQ-9: t=5.34, p<0.001). Among 43 participants with baseline MRS data, no group differences were seen for metabolite indices when comparing those with and without depression or anxiety.

We incorporated all psychiatric data for time since diagnosis, which is also time on cART, into multivariable linear regressions that included baseline CD4 count, plasma HIV RNA, and plasma neopterin. Only baseline plasma neopterin correlated with scores on all psychiatric measures (HADS-A: t=2.65, p=0.014; HADS-D: t=2.94, p=0.007; PHQ-9: t=3.57, p=0.001). Time since diagnosis, which also reflects time on cART, was a relevant factor for improved scores on the HADS-A (t=−2.29, p=0.030) and HADS-D (t=−2.90, p=0.008) scores.[1]

DISCUSSION

We identified a high frequency of clinically relevant anxiety and depressive symptoms during AHI prior to starting cART. The presence of clinically relevant psychiatric symptoms at study entry in AHI was associated with worse measures of blood-derived, but not CSF-derived, markers of HIV infection and immune dysfunction. However, in fully adjusted models plasma neopterin, a marker of macrophage activation, was the only factor that remained significant. Our findings confirm that biological factors related to HIV infection associate with the presence of psychiatric symptoms during untreated acute HIV infection. Additionally, the presence of clinically relevant affective symptoms significantly improved during the six-month follow-up period after initiation of cART, and began to approach rates in HIV negative individuals. This may, in part, be due to cultural factors of the Thai participants. Although the rates of depression and anxiety in HIV-negative Thais have not been published, Thai primary care providers have projected that up to 35% of all of their patients have any psychiatric illness [48]. The lifetime prevalence of a major depressive episode among Thais has been reported as 19.9%, with anxiety disorders at 10.2% [49]. We did not have access to a control group, and future studies would be strengthened by comparing these findings to a HIV negative group undergoing a similarly stressful life event.

The uniform timing of our study ensured that at study entry, participants had a shared temporal experience of receiving a HIV diagnosis, were in a similar biological phase of disease, and similarly lacked exposure to antiretroviral therapy. Adding value, our participants were relatively similar in terms of demographic factors that may influence psychiatric symptom burden, providing a homogeneous background to assess the influence of HIV-related factors. For example, our participants shared similar cultural and educational backgrounds, were primarily young men who identified as MSM, were without serious pre-existing medical or psychiatric disease prior to study entry, and were all naïve to cART at the first assessment. These factors contributed to our ability to discern a significant association with plasma neopterin, a marker of macrophage activation, and psychiatric symptoms in the

[1]As immune activation can be influenced by hormone changes, we completed sensitivity analyses removing from the dataset all cisgender women (n=5), as well as transgender women (n=3) who may have been taking hormone supplementation. We found no substantial differences in the reported outcomes. Significance was lost on correlation between baseline HADS-A anxiety score and CD4 count at baseline (p=0.066, r=−0.17, n=115) likely owing to a reduced sample size, as a trend towards significance remains. Additionally, all statistical models were re-run including gender as a covariate to examine any differential effect gender would have on the other covariates or the outcome. Gender was not a significant covariate in any of the models.

current study. Given that immune activation may be influenced by hormonal changes, a repeat analysis restricted to male sex (eliminating cisgender and transgender women) did not substantially influence any of our findings.

We observed different blood immunologic states in participants with clinically relevant depressive symptoms at HIV diagnosis, consistent with prior studies suggesting that immunologic factors correlate with depression. A meta-analysis of 24 studies in the general population found higher levels of plasma pro-inflammatory cytokines (IL-6 and TNF-α) in people meeting DSM-IV criteria for depression compared to those that did not [50]. The causal relationships are unknown, although it has been hypothesized that chronic depression may induce immune activation. Individuals with multiple sclerosis, an autoimmune disease of the CNS, report depression at elevated rates [51, 52, 53]. This depression can precede overt neurological symptoms, suggesting that inflammation and brain damage are linked to affective disturbance for some individuals with multiple sclerosis. While we found an association between plasma neopterin and affective symptoms prior to treatment, it is notable that plasma neopterin has been shown to reduce with cART initiation, but not down to levels of HIV-negative individuals, even after one year of treatment [54].

A strength of the present study was the utilization of depression and anxiety measures that have been previously validated for administration in Thailand [10, 43]. The measures generated slightly different results, likely due to the design and sensitivity of the two instruments. For example, the HADS excludes questions about somatic symptoms, and the PHQ-9 is based more closely on DSM-IV criteria for depression. The inclusion of somatic symptoms on the PHQ-9 would explain why participants meeting depression criteria at diagnosis also exhibited more symptoms of ARS. It is possible that these individuals experienced more severe reactive mood disturbance secondary to these physical symptoms of HIV. However, this argument is mitigated by the independent associations between HADS-D and disease biomarkers, as the HADS-D did not associate with ARS. Use of both measures in this study adds depth to our understanding of depression in AHI.

There are many factors that may contribute to symptoms of depression and anxiety in acute HIV, including a stress reaction to the recent diagnosis [12]. The associations between baseline scores on the Distress Thermometer and the baseline HADS-A anxiety, HADS-D depression, and the PHQ-9 depression scores implies that we cannot rule out the degree to which these baseline affective symptoms were related to concurrent distress. However, the associations between depression and anxiety scores and increased plasma immune activation support that there is a biological component to the degree of symptoms. It is notable that due to the time and resource limitations of the parent study design, we were not able to establish definitive psychiatric diagnoses of depression or anxiety at the time points in the presented work. Instead, we used published thresholds on screening assessments to examine the presence of clinically relevant depression and anxiety symptoms.

Similar to previous reports of affective symptoms in acute and early HIV [14], we identified frequent, clinically relevant depressive symptoms, and even higher rates of clinically relevant anxiety symptoms. Unlike previous reports, in our study, the presence of clinically relevant depressive and anxiety symptoms decreased concurrent with cART treatment, and

this finding was sustained at six months. Our study did not include a comparison group of individuals not taking cART, and therefore we cannot speculate on the effects of cART on affective symptoms. Despite improvement in affective symptoms over time, some participants had severe self-reported depression or anxiety symptoms at study entry, and one participant died by suicide over three and a half years into the study. Results from the study emphasize the importance of clinical attention to affective symptoms soon after individuals receive a diagnosis of HIV, and the need for healthcare providers to cultivate networks of support and treatment for their patients.

It is notable that efavirenz can have neuropsychiatric side effects, and all participants in this study were started on an efavirenz based regimen. The design of the parent study benefits from having obtained study entry data just prior to starting combination antiretroviral therapy. Thus, is it possible that measures of psychiatric symptoms from week 4 onwards were inflated due to use of efavirenz. However, this is unlikely as of the severity of symptoms for both depression and anxiety declined over time.

Although 25% of participants reported drug use in the four months preceding study entry, the majority of these cases were characterized by sporadic, recreational use of drugs such as amyl nitrites (“poppers”) during sexual encounters, and the rate of drug use did not differ in those with or without clinically relevant anxiety or depressive symptoms. As we only had access to plasma neopterin levels on 12 participants at follow up, we lacked sufficient power to examine longitudinal influences of immunologic markers on depression and anxiety. This will be explored in future projects, as well as other potential contributors, such as levels of microbial translocation. Other limitations include the small number of CSF samples, which limited the opportunity to detect associations with CNS immune factors. Also, we did not assess the presence of PTSD in this study. Finally, the homogeneity of our participants restricts generalizability of the results, but increases the internal validity and stability of our findings.

In summary, we identified high rates of clinically relevant anxiety and depression symptoms following diagnosis of acute HIV infection, confirming this period as a time of high risk for significant affective symptoms. While many variables contribute to the presence of affective symptoms, we observed a significant relationship between elevated baseline plasma neopterin, a marker of macrophage activation, and clinically relevant symptoms of depression and anxiety during untreated acute HIV infection. Future studies are needed to determine if certain factors associate with the persistence of depression and anxiety symptoms after treatment, and whether symptoms can improve with interventions targeting viral activity and immune dysregulation.

Acknowledgments

We thank our study participants and staff from the Thai Red Cross AIDS Research Centre and the Silom Community Clinic in Bangkok, and the Early Capture HIV Cohort (ECHO) Center in Pattaya, Thailand for their valuable contributions to this study. RV254/SEARCH is a research collaboration between the Thai Red Cross AIDS Research Centre (TRCARC), the University of California San Francisco, the University of Hawaii, and the Department of Retrovirology, US Army Medical Component, Armed Forces Research Institute of Medical Sciences (USAMC-AFRIMS), and the U.S. Military HIV Research Program at the Walter Reed Army Institute of Research. The SEARCH 010 Study Group also includes the following individuals: Praphan Phanuphak, MD, PhD (SEARCH, TRCARC, clinical investigator); Nittaya Phanuphak, MD, PhD (SEARCH, principal investigator); Eugene Kroon,

MD, MPH (SEARCH, clinical investigator); Carlos Secdalan, MD (SEARCH, clinical investigator); Nitiya Chomchey, MSc, (SEARCH, study coordinator); Somprartthana Rattanamanee, MSc (SEARCH, research nurse); Puttachard Sangtawan, BNS (SEARCH, research nurse); Bessara Nuntapinit, BSc (AFRIMS, lead of specimen processing team); Phiromrat Rakyat, BSc (AFRIMS, specimen processing); Surasit Inprakong, BSc (AFRIMS, specimen processing); Sukanya Lucksanawong, BSc (AFRIMS, specimen processing); Panjaree Ruangjan, MPH (AFRIMS, specimen processing); Anake Nuchwong, BSc (AFRIMS, specimen processing); Panadda Kruacharoen, BSc (AFRIMS, specimen processing); Robert O'Connell, MD (AFRIMS, clinical investigator); Collin Adams, BS (UCSF, study coordinator); Katherine Clifford, BA (UCSF, study coordinator); Leah Le, MPH (Yale University, study coordinator); Hetal Mistry, BS (Yale University, research associate); Sodsai Tovanabutra, PhD (Military HIV Research Program, lab investigator); Suteeraporn Pinyakorn, MSc (Military HIV Research Program, statistician); Merlin Robb, MD (Military HIV Research Program, clinical investigator).

Funding: This study was funded by the National Institutes of Health (R01MH095613, R21MH086341, R01MH09561302-S1, R01NS061696) and the US Military HIV Research Program, Walter Reed Army Institute of Research, Rockville, Maryland, under a cooperative agreement between the Henry M. Jackson Foundation for the Advancement of Military Medicine, Inc., and the U.S. Department of Defense (W81XWH-07-2-0067), with added support from the National Institutes of Mental Health.

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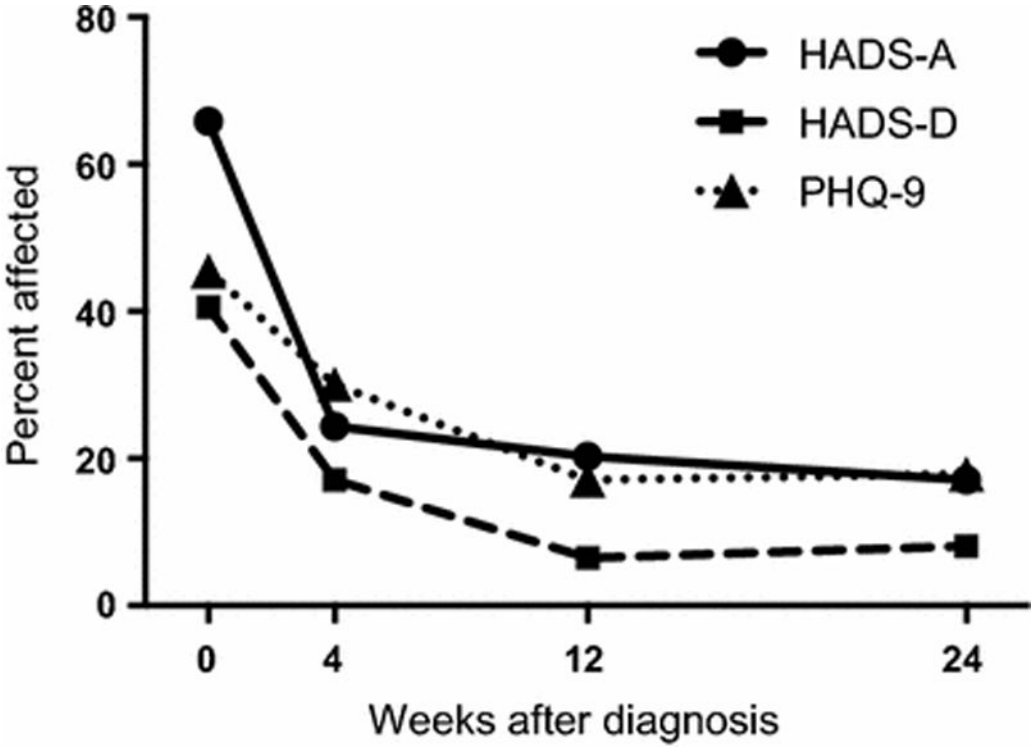

Figure 1.
Frequency of clinically relevant anxiety and depression, by mood inventory, following acute HIV diagnosis.

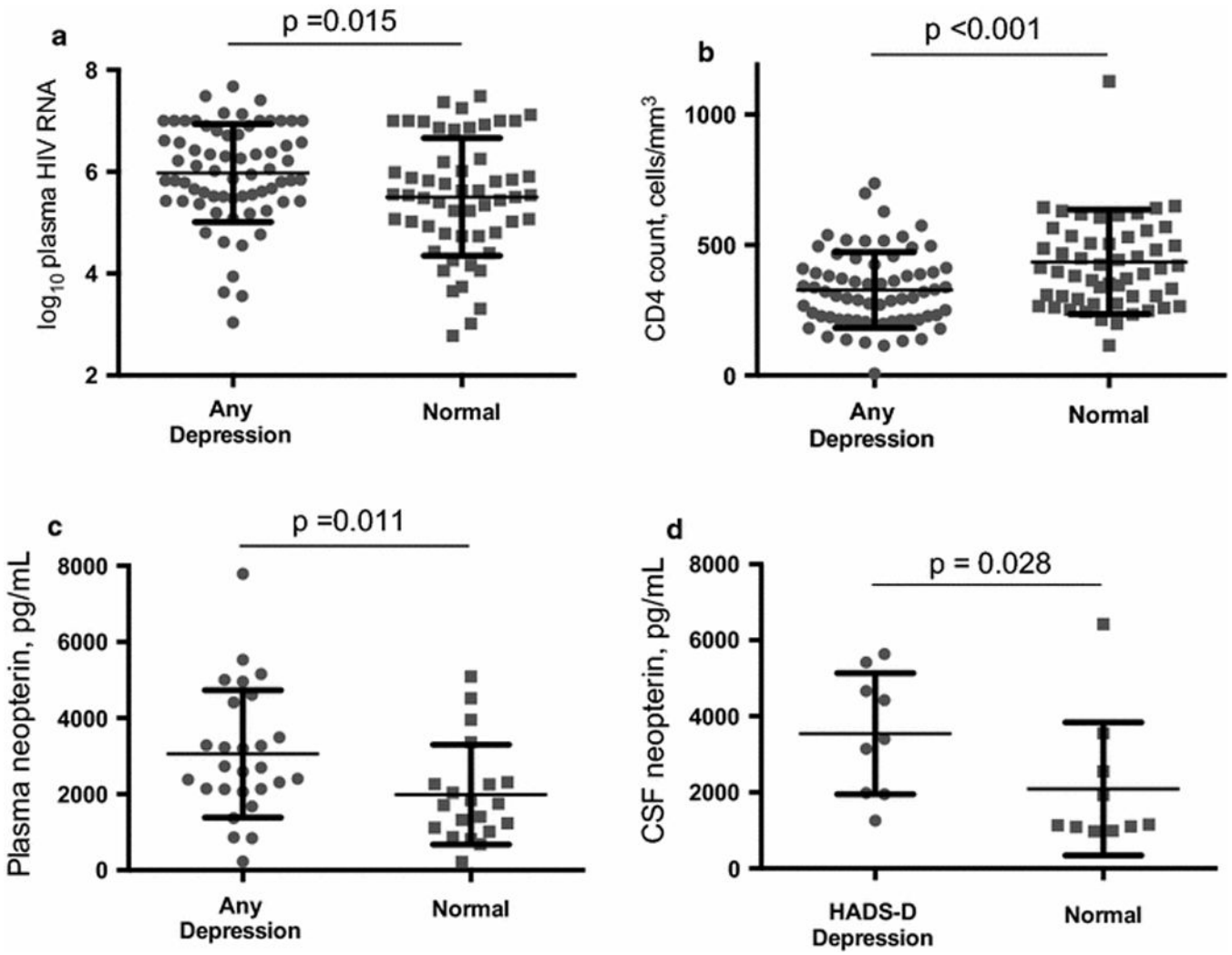

Figure 2.

Presence of depression at study entry and markers of HIV infection. (A) Plasma HIV RNA for those participants with depression on at least one measure at week 0 visit compared to those within normal week 0 depression scores on both measures. (B) CD4 count for those meeting depression thresholds on at least one measure at week 0 visit compared to those within normal week 0 depression scores on both measures. (C) Plasma neopterin for participants with depression on at least one measure at week 0 visit compared to those within normal depression scores at week 0 on both measures. (D) CSF neopterin for participants with depression on the HADS-D at week 0 visit, compared to those within normal week 0 depression scores.

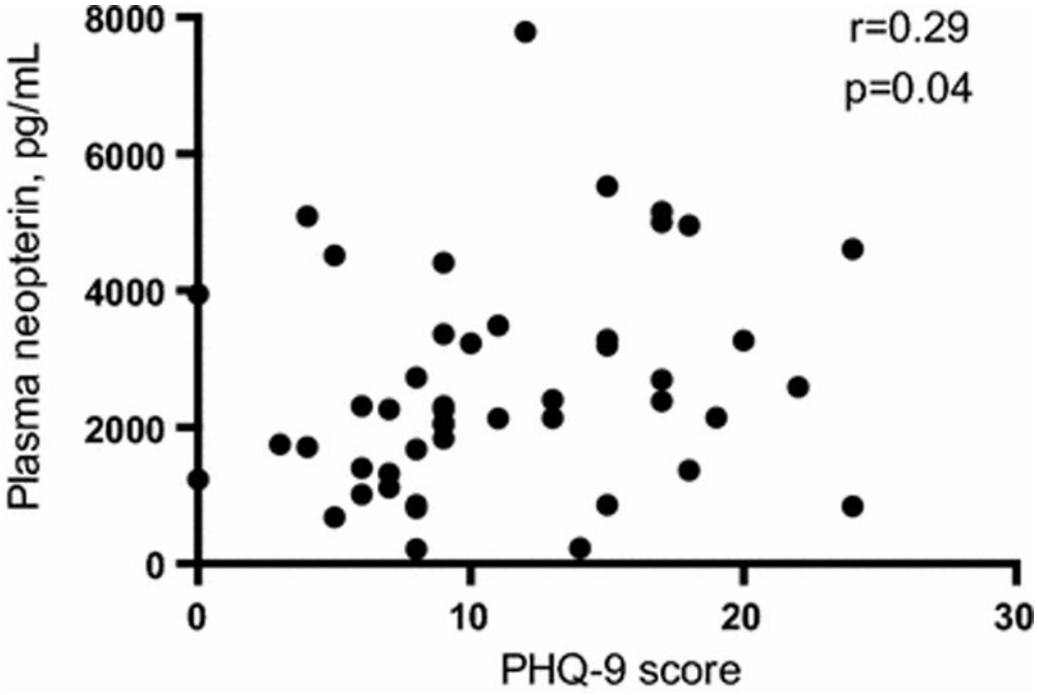

Figure 3.
Correlation of PHQ-9 depression score and plasma neopterin levels.

Table I

AHI participant demographics by presence of depression at study entry.

	All participants	No depression at study entry	Depression at study entry	p-value
Number of participants (%)	123	55 (45)	68 (55)	–
Age, years (range/IQR)	28 (18–53)	29 (10)	27 (9)	0.121
Education, years (range/IQR)	16 (2–24)	16 (4)	16 (3)	0.980
EID, days (range/IQR)	19.8 (3–59)	20.4 (11)	19.3 (11)	0.501
% Male participants	94	96	92	0.246
% in Fiebig stage I/II	49	58	42	0.061
% in Fiebig stage III-V	51	42	58	0.061
% with drug use	25	20	26	0.874
% on augmented cART+ regimen	48	47	49	0.890
CD4+, cells/mm^3 (range/IQR)	376 (7–1236)	436 (242)	328 (197)	<0.001 *
Plasma log_{10} HIV RNA (range/IQR)	5.8 (2.8–7.7)	5.5 (1.5)	6.0 (2.3)	0.015 *
CSF log_{10} HIV RNA (range/IQR)	3.6 (2–5.5)	3.2 (2.2)	4.0 (3.2)	0.118

Demographic means for AHI participants and without depression at diagnosis (meeting threshold criteria on either HADS-D or PHQ-9). AHI = acute HIV infection; IQR = interquartile range; EID = estimated infection duration at study entry.

* $p<0.05$ between participants with and without depression at study entry.