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REVIEW ARTICLE

MIND AND IMMUNITY: EXPLORING THE INTERPLAY BETWEEN HIV AND MENTAL HEALTH DISORDERS - A REVIEW

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Abstract

HIV infection has long been recognized for its profound effects on the immune system, but growing evidence highlights its significant impact on mental health as well. Individuals living with HIV are disproportionately affected by psychiatric conditions such as depression, anxiety, and HIV-associated neurocognitive disorders (HAND). These mental health challenges not only arise from the psychosocial burden of chronic illness and stigma but are also rooted in the biological interactions between HIV and the central nervous system (CNS). The virus infiltrates the CNS early in infection, triggering a cascade of neuroinflammatory processes that contribute to neuronal damage and neurotransmitter dysregulation. Chronic immune activation, marked by elevated cytokines and systemic inflammation, plays a key role in the pathogenesis of mental health disorders in HIV-positive individuals. Conversely, psychological distress can impair immune function, reduce CD4+ T-cell counts, and undermine adherence to antiretroviral therapy (ART), thereby accelerating disease progression and compromising overall health outcomes.

Keywords: Depression, HIV, immune dysregulation, mental health, neuroinflammation.

INTRODUCTION

The human immunodeficiency virus (HIV) remains one of the most formidable global health challenges, affecting over 38 million people worldwide[1,2]. Advances in antiretroviral therapy (ART) have dramatically improved the prognosis of people living with HIV (PLWH), transforming what was once a fatal disease into a manageable chronic condition[3-4]. However, as the life expectancy of HIV-infected individuals' increases, a more complex spectrum of comorbidities has emerged chief among them are mental health disorders[5-6]. The intersection between HIV and mental health has gained increasing attention due to its significant implications for disease progression, treatment adherence, and overall quality of life. Mental health disorders, particularly depression and anxiety, are substantially more prevalent among PLWH compared to the general population. These psychiatric conditions are not merely coincidental but are deeply intertwined with the experience of living with HIV. Stigma, social isolation, fear of disclosure, and financial instability contribute to psychological distress. Moreover, the chronic nature of the disease and its potential to impair physical functioning can result in long-term emotional burden and diminished self-worth. Beyond psychosocial factors, emerging evidence points to a biological basis for mental health disturbances in HIV-infected individuals. HIV penetrates the central nervous system (CNS) early in infection, where it establishes viral reservoirs in microglia and macrophages. This neuroinvasion results in persistent neuroinflammation, oxidative stress, and synaptic injury, which are strongly associated with psychiatric symptoms and cognitive decline. The brain's immune response to the virus may, in fact, mirror inflammatory processes observed in primary mental illnesses[7-11].

Neuroinflammation triggered by HIV plays a critical role in altering neurotransmitter function. Elevated levels of pro-inflammatory cytokines such as tumor necrosis factor-alpha (TNF-α), interleukin-6 (IL-6), and interferon-gamma (IFN-γ) are linked to disruptions in serotonin, dopamine, and glutamate pathways—all of which are crucial in mood regulation and executive functioning[12-14]. These biochemical changes can manifest as depression, apathy, irritability, and cognitive impairment, forming the clinical picture commonly seen in HIV-associated neurocognitive disorders (HAND). Conversely, mental health conditions may also negatively influence immune function[15,16]. Depression and chronic stress have been

shown to impair the hypothalamic-pituitary-adrenal (HPA) axis and diminish the activity of natural killer cells, reducing the body's ability to mount an effective immune response[17,18]. In the context of HIV, this immunosuppression can contribute to faster CD4+ T-cell decline, higher viral loads, and increased vulnerability to opportunistic infections. Therefore, the mind-immune interface is not unidirectional but constitutes a dynamic and reciprocal relationship[19,20]. The presence of psychiatric symptoms in PLWH has also been linked to poor ART adherence, which is a critical determinant of viral suppression and long-term health outcomes. Individuals suffering from untreated depression or anxiety are less likely to engage with healthcare systems, adhere to medication regimens, or attend regular follow-up appointments. Consequently, mental health disturbances may indirectly contribute to HIV disease progression and limit the success of public health interventions aimed at controlling the epidemic[21,22].

This review aims to explore the complex bidirectional relationship between mental health disorders and immune function in individuals living with HIV.

Screening and selection of studies

Initial screening of titles and abstracts was conducted to exclude irrelevant studies. Studies that focused solely on HIV treatment, without examining mental health outcomes or immune responses, were excluded. Following this, full-text articles were reviewed to assess relevance to the review's scope. A total of 55 studies met the inclusion criteria, including both observational studies and randomized controlled trials, covering various mental health conditions such as depression, anxiety, HIV-associated neurocognitive disorders (HAND), and substance use disorders. Studies were selected based on their rigor, sample size, and relevance to the understanding of the bidirectional relationship between HIV and mental health.

Prevalence and types of mental health disorders in HIV patients

Mental health disorders are strikingly prevalent among individuals living with HIV, with various studies consistently reporting higher rates of psychological morbidity compared to the general population. This elevated burden of mental illness spans a wide spectrum of conditions, including depression, anxiety, substance use disorders, post-traumatic stress disorder (PTSD), and HIV-associated neurocognitive disorders (HAND).[23-25] These psychiatric conditions do not occur in isolation; rather, they are often co-occurring, chronic, and intricately linked with the biological and psychosocial challenges of living with a stigmatized, life-altering illness. Depression is one of the most commonly reported mental health conditions in people living with HIV, with global prevalence estimates ranging from 30% to 50%, depending on the population and method of diagnosis[26-28]. The rate is significantly higher than the estimated 7% prevalence in the general population, highlighting a disproportionate vulnerability. Factors contributing to this include the psychological stress of diagnosis, fear of disease progression, internalized stigma, social isolation, and economic hardship[29]. Depression in HIV patients is not only common but also particularly debilitating, often leading to impaired medication adherence, diminished functional capacity, and poor health-related quality of life[30]. It is also associated with increased risk of suicide and accelerated disease progression due to its impact on the immune system.

Anxiety disorders are also highly prevalent in HIV-infected populations. Generalized anxiety disorder, panic disorder, and social anxiety frequently manifest in patients struggling with the uncertainties of living with a chronic, potentially fatal illness. The fear of disclosure, discrimination, and rejection can exacerbate anxious symptoms and foster maladaptive coping strategies. Anxiety, like depression, can interfere with decision-making, reduce treatment engagement, and increase risky behaviors such as substance use or unprotected sex, thereby posing additional public health risks[31-33].

Substance use disorders, including alcohol dependence and illicit drug use, are particularly concerning in the context of HIV. In some cases, substance abuse precedes HIV infection through high-risk behaviors such as needle sharing or unprotected intercourse. In other instances, individuals turn to drugs or alcohol as a coping mechanism after diagnosis. The presence of substance use disorders complicates treatment, impairs judgment, and has been associated with lower ART adherence, increased viral replication, and poorer health outcomes. Dual diagnosis co-occurrence of psychiatric illness and substance use adds an additional layer of complexity to management[34-37]. Post-traumatic stress disorder (PTSD) is another significant but often under-recognized condition among HIV-positive individuals. Many patients experience traumatic events related to the diagnosis itself, such as disclosure-related violence, loss of social support, or historical trauma from abuse or homelessness. PTSD symptoms—such as flashbacks, hyperarousal, and emotional numbing—can further impair adherence to medical care and undermine therapeutic relationships. In vulnerable populations such as women, children, and men who have sex with men (MSM), the prevalence of PTSD may be even higher due to intersecting forms of trauma and marginalization. Perhaps most unique to the HIV population is the occurrence of HIV-associated neurocognitive disorders (HAND), which encompass a range of cognitive impairments linked to the direct and indirect effects of the virus on the central nervous system[38-40]. HAND includes three subtypes: asymptomatic neurocognitive impairment (ANI), mild neurocognitive disorder (MND), and the most severe form, HIV-associated dementia (HAD). These conditions may affect memory, attention, executive functioning, and psychomotor speed, often impacting patients' ability to manage daily tasks and adhere to treatment regimens. While the incidence of HAD has declined significantly in the ART era, milder forms of cognitive dysfunction remain common, especially among individuals with delayed diagnosis, low CD4 counts, or a history of substance abuse[41-43].

The prevalence and diversity of mental health disorders among HIV-positive individuals underscore the importance of routine psychiatric screening and early

intervention. Mental health is a critical yet frequently neglected component of comprehensive HIV care. Failure to address psychological comorbidities not only impairs quality of life but also jeopardizes the long-term success of ART and the broader goals of HIV control and prevention. A deeper understanding of the types and frequencies of mental illness in this population can inform the development of more holistic, integrated care strategies that truly meet the multifaceted needs of people living with HIV[44-46].

Neuroimmunological mechanisms of interaction

The complex interplay between HIV and mental health disorders is rooted in a series of neuroimmunological mechanisms that reflect the virus's capacity to dysregulate both the immune and nervous systems. Unlike many other viral infections, HIV has the ability to penetrate the central nervous system (CNS) early during acute infection, establishing viral reservoirs in resident immune cells such as microglia and macrophages[47,48]. Once within the CNS, HIV triggers a cascade of neuroinflammatory responses that persist despite effective antiretroviral therapy (ART), contributing to the pathophysiology of various psychiatric and neurocognitive disorders. A hallmark of HIV neuropathogenesis is chronic immune activation. HIV infection is associated with sustained systemic and CNS inflammation, characterized by the overproduction of pro-inflammatory cytokines, including tumor necrosis factor-alpha (TNF-α), interleukin-1 beta (IL-1β), interleukin-6 (IL-6), and interferon-gamma (IFN-γ). These cytokines can cross the blood-brain barrier or be produced locally within the CNS, altering neurotransmitter metabolism, synaptic plasticity, and neuronal survival[49,50]. For instance, elevated levels of TNF-α and IL-6 have been implicated in the disruption of serotonin and dopamine pathways, both of which are critical in mood regulation and cognitive function. This biochemical dysregulation provides a direct biological link between HIV infection and symptoms of depression, anxiety, and cognitive decline. In addition to cytokine-mediated neurotoxicity, the infiltration and activation of immune cells in the brain contribute to neuronal injury. Activated microglia and astrocytes release neurotoxic substances such as nitric oxide, reactive oxygen species, and excitatory amino acids like glutamate, leading to oxidative stress and excitotoxicity. These processes result in dendritic pruning, synaptic loss, and neuronal apoptosis—key features observed in both HIV-associated neurocognitive disorders (HAND) and major depressive disorder. Notably, these changes occur even in the absence of detectable viral replication in the CNS, underscoring the enduring impact of immune-mediated injury[51-53].

Another critical mechanism involves the dysregulation of the hypothalamic-pituitary-adrenal (HPA) axis. Chronic inflammation and psychological stress associated with HIV can disrupt the HPA axis, leading to abnormal cortisol secretion. Elevated cortisol levels, in turn, suppress immune function and exacerbate depressive symptoms, creating a self-perpetuating cycle of immune and neuroendocrine dysfunction[54,55]. Furthermore, HIV-related inflammation has been shown to impair neurogenesis in the hippocampus a brain region essential for memory and emotion regulation thus contributing to cognitive and affective symptoms observed in PLWH. The role of monocyte trafficking across the blood-brain barrier is also central to the neuroimmune interaction in HIV[56,57]. Infected monocytes serve as "Trojan horses", ferrying HIV into the CNS, where they differentiate into perivascular macrophages and propagate local inflammation. The ongoing recruitment and activation of these cells fuel the neurodegenerative process and maintain the CNS as a sanctuary site, even during suppressive ART[58]. This reservoir function limits the effectiveness of systemic therapy and poses a significant challenge to viral eradication efforts. Importantly, the effects of HIV on neuroimmune dynamics may be modulated by host genetic factors, co-infections (e.g., hepatitis C virus, cytomegalovirus), substance use, and social determinants of health. These factors can influence individual susceptibility to neuropsychiatric outcomes, adding layers of complexity to diagnosis and management. For example, individuals with a history of methamphetamine use or co-morbid post-traumatic stress may experience exacerbated neuroinflammation and more severe cognitive impairments[59].

Bidirectional relationship between mental health and immunity

The relationship between mental health and immunity in the context of HIV is not unidirectional but rather characterized by a complex, reciprocal interplay. On one hand, HIV-induced immune dysregulation directly contributes to the development of mental health disorders; on the other hand, psychiatric conditions such as depression and chronic stress can negatively influence immune function, creating a feedback loop that exacerbates disease progression and undermines treatment outcomes. This bidirectional model underscores the necessity of an integrative approach to care, recognizing the interdependence of psychological and immunological health in people living with HIV (PLWH). From the immunological standpoint, HIV infection leads to profound alterations in both innate and adaptive immune responses. Chronic systemic inflammation, immune activation, and progressive CD4+ T-cell depletion are central features of HIV pathogenesis[60,61]. These immune abnormalities extend to the central nervous system (CNS), where they promote neuroinflammation and contribute to the onset of mood disorders and cognitive impairment. For instance, elevated levels of interleukin-6 (IL-6), C-reactive protein (CRP), and tumor necrosis factor-alpha (TNF-α) have been associated with depressive symptoms in HIV-positive individuals. These pro-inflammatory cytokines interfere with monoamine neurotransmitter synthesis, impair neuroplasticity, and disrupt the regulation of the hypothalamic-pituitary-adrenal (HPA) axis, leading to a physiological environment conducive to mental illness. Conversely, mental health disorders exert significant effects on immune competence. Chronic psychological stress, depression, and anxiety are known to modulate immune responses via the HPA axis and sympathetic nervous system. Persistent activation of these stress

pathways results in elevated cortisol and catecholamine levels, which suppress cellular immunity, reduce natural killer (NK) cell activity, and impair lymphocyte proliferation. In PLWH, such immune suppression may accelerate viral replication, reduce CD4+ T-cell counts, and increase vulnerability to opportunistic infections and non-AIDS-related comorbidities. Furthermore, mental health conditions can alter the expression of genes involved in inflammation and immune signaling, a phenomenon observed in psychoneuroimmunology studies, adding another layer of complexity to immune dysregulation in HIV[62].

Behavioral mechanisms further amplify this immunological impact. Mental health disorders often lead to reduced adherence to antiretroviral therapy (ART), poor engagement with health services, substance abuse, and risky sexual behavior. These behaviors not only compromise treatment effectiveness but also promote viral resistance and community transmission. Depression, in particular, is strongly associated with ART non-adherence, which can result in increased viral load, immune deterioration, and more severe neurocognitive consequences. In turn, poor health outcomes can deepen psychological distress, completing a vicious cycle of immune and mental health decline. This reciprocal dynamic is also influenced by socioeconomic and structural determinants of health, including stigma, poverty, social isolation, and trauma. These factors disproportionately affect HIV-positive populations, especially marginalized groups such as women, adolescents, LGBTQ+ individuals, and people who use drugs. The psychosocial stressors they endure are tightly linked with both increased psychiatric morbidity and immune dysregulation, further entrenching health disparities. Addressing these social determinants is essential for breaking the feedback loop between mental illness and immune dysfunction in HIV care. The bidirectional relationship between mental health and immunity has profound clinical implications. It challenges the conventional compartmentalization of HIV care into distinct medical and psychiatric domains and calls for a more integrated, biopsychosocial model of treatment. Interventions that simultaneously address mental health and immune health—such as combining ART with cognitive-behavioral therapy, psychotropic medications, or mindfulness-based stress reduction may offer synergistic benefits. Moreover, routine screening for depression, anxiety, and substance use should be considered standard practice in HIV management, with appropriate referral pathways for psychological support[63,64].

Clinical implications and the need for integrated care

The intricate relationship between HIV and mental health has far-reaching clinical implications, demanding a paradigm shift in how care is conceptualized and delivered to people living with HIV (PLWH). As evidence accumulates on the bidirectional nature of mental illness and immune dysfunction, it becomes increasingly clear that conventional siloed approaches to treatment are inadequate. Mental health disorders ranging from depression and anxiety to substance use and neurocognitive impairment are not only frequent in PLWH but significantly influence disease progression, treatment adherence, quality of life, and overall morbidity and mortality. These realities underscore the necessity for an integrated model of care that concurrently addresses the psychological, neurological, and immunological dimensions of HIV. One of the most pressing clinical implications is the impact of mental health disorders on adherence to antiretroviral therapy (ART). Numerous studies have demonstrated that individuals with untreated depression or anxiety are significantly less likely to initiate or maintain ART, contributing to increased viral load, CD^{4+} T-cell decline, and heightened risk of opportunistic infections. Additionally, psychiatric symptoms can interfere with patients' ability to attend clinic appointments, communicate effectively with healthcare providers, and engage in preventative health behaviors. This creates a compounding cycle in which untreated mental illness exacerbates HIV progression, which in turn deepens psychological distress. Furthermore, neurocognitive disorders associated with HIV collectively referred to as HIV-associated neurocognitive disorders (HAND) pose diagnostic and therapeutic challenges. These disorders range in severity from asymptomatic neurocognitive impairment to HIV-associated dementia, and they can profoundly impair memory, executive function, and motor coordination. Early identification of HAND is often overlooked due to limited screening resources or the misattribution of symptoms to aging or psychiatric comorbidities. Left unaddressed, these impairments can hinder medication management, increase dependency, and reduce functional independence[65-67].

In this context, integrated care models become not just beneficial, but essential. Integrated care involves the systematic coordination of general medical, mental health, and social services within a unified clinical framework. For PLWH, this means co-locating mental health professionals in HIV clinics, implementing routine screening for psychological disorders, and fostering multidisciplinary collaboration among infectious disease specialists, psychiatrists, psychologists, social workers, and case managers. Such models have demonstrated improved ART adherence, reduced hospitalization rates, and enhanced patient satisfaction and retention in care. Moreover, integrated care should be culturally competent and sensitive to the unique psychosocial realities faced by PLWH, especially among marginalized populations. This includes addressing issues of stigma, discrimination, trauma history, housing instability, and substance use all of which act as barriers to both mental health and HIV care. Tailored interventions, such as trauma-informed care and harm reduction strategies, can help build trust and promote engagement among vulnerable groups. Integrating peer support programs and community-based outreach has also been shown to improve outcomes and foster resilience. Policy-level support is equally crucial. Many healthcare systems operate with fragmented funding streams that separate mental health from primary or HIV care, discouraging

a unified approach. Health policymakers must prioritize integrated service delivery through targeted funding, training, and the development of collaborative care models[68]. Reimbursement structures should incentivize multidisciplinary practices, and medical curricula must incorporate training on the intersection of mental health and infectious disease. Research must continue to refine and evaluate integrated care strategies[69]. There remains a need for evidence on the effectiveness of specific interventions in various cultural and socioeconomic contexts, as well as for innovative models that leverage digital health technologies to expand mental health access. Mobile health (mHealth) tools, telepsychiatry, and electronic health record integration offer promising avenues for delivering mental health support alongside HIV care, particularly in resource-limited settings[70].

CONCLUSIONS

This review highlights the critical and often overlooked intersection between HIV and mental health disorders, underscoring the complex, bidirectional relationship between psychological well-being and immune function in individuals living with HIV. Mental health conditions, including depression, anxiety, substance use, and HIV-associated neurocognitive disorders, significantly impact both the clinical management of HIV and the overall health outcomes of those affected. Through an exploration of neuroimmunological mechanisms, it has become evident that immune dysregulation in HIV exacerbates psychiatric symptoms, while mental health disorders, in turn, accelerate immune dysfunction, impair treatment adherence, and increase the burden of comorbidities. The review emphasizes the urgent need for integrated care models that simultaneously address both HIV and mental health needs. Effective care for people living with HIV must not only focus on antiretroviral therapy and immune system management but also provide comprehensive mental health services to improve ART adherence, reduce disease progression, and enhance quality of life. This approach is particularly essential given the psychosocial challenges faced by PLWH, such as stigma, discrimination, and social marginalization, which further complicate their mental health and immune responses.

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AUTHOR'S CONTRIBUTION

Obeagu EI: conceived the idea, writing the manuscript, literature survey. **Alsadi RA:** formal analysis, critical review. Final manuscript was checked and approved by the both authors.

DATA AVAILABILITY

Data will be made available on request.

CONFLICT OF INTEREST

There are no conflicts of interest in regard to this project.

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