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Psychiatric Comorbidities in HIV-Positive Patients: A Literature Review

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Abstract

Background People living with HIV (PLWH) experience psychiatric comorbidities far more frequently than the general population, with prevalence estimates ranging from 1.5 to 8 times higher. These mental health conditions substantially impact treatment adherence, viral suppression, and overall quality of life.

Aim This literature review aimed to provide an updated, comprehensive overview of psychiatric comorbidities in people living with HIV and their underlying biological and psychosocial mechanisms.

Materials and Methods This article systematically reviews the existing literature on psychiatric comorbidities among HIV-positive patients. A comprehensive database search was conducted using Web of Science, PubMed, and Google Scholar. The bibliographies of cited works were also reviewed. The literature review and article selection process concluded in October 2025.

Results To the most prevalent psychiatric disorders among PLWH belong depression (31%), posttraumatic stress disorder – PTSD (28%), anxiety disorders (20-40%), substance use disorders – SUD (40-74%), and HIV-associated neurocognitive disorders – HAND (45%). Psychiatric comorbidities in PLWH result from complex interactions between biological mechanisms – including HIV's affinity for neural tissue, chronic neuroinflammation mediated by cytokines such as IL-6 and TNF-α, and reduced monoamine availability – and psychosocial factors, particularly internalized stigma, discrimination, and trauma related to HIV diagnosis.

Conclusions Early health screening and implementation of mental health services within HIV treatment improve psychiatric outcomes and ART adherence.

Keywords: HIV, depression, PTSD, anxiety, substance use disorders, neurocognitive disorders

Introduction

HIV remains a global health issue. Approximately 40.8 million people worldwide are living with HIV, with around 1.3 million new infections occurring in 2024. Since 2010, the number of deaths caused by this virus has fallen by 54%, which is due to greater awareness and wider access to antiretroviral therapy (ART) [1]. For this reason, in the context of HIV, there is increasing talk not only of inhibiting replication but also of its impact on the overall health and well-being of patients. The mental health of patients living with HIV (PLWH) is crucial in the overall approach to their care, as the coexistence of mental illness with HIV infection can worsen patients' clinical outcomes. It has been shown that the coexistence of HIV with mental illness contributes to increased mortality due to increased difficulties in taking antiretroviral drugs (medication adherence). Treatment of mental illness in these patients improves ART adherence. [2] For this reason, understanding the importance of mental health in these patients is crucial to the development of a comprehensive and effective care strategy.

Epidemiological studies have shown that mental illness is 1.5 to 8 times more common in PLWH than in the general population [3]. The most commonly reported mental health problems and disorders include depression (31%), PTSD (28%), and anxiety disorders (20-40%), substance use disorder (40-74%), HIV-associated neurocognitive disorders (HAND) (45%), and psychosocial factors (stigmatization, community support, socioeconomic status) [2]. Understanding such a multitude and complexity of factors is essential for optimizing care for HIV-positive patients.

The co-occurrence of mental illness in PLWH is caused by the complex interaction of many factors, primarily biological, psychological, and social. Biological factors include, above all, the enormous affinity of HIV for nervous tissue. Many studies have shown that brain volume is reduced in PLWH. The results of these studies agree that the virus causes brain atrophy. The region of the brain most commonly associated with neurodegenerative disorders in HIV patients is the caudate nucleus, damage to which is primarily responsible for the development of HAND. [4] Psychological and social factors responsible for the development of mental illness include low self-esteem caused by stigmatization, rejection, loss of social identity, and psychosocial mechanisms such as chronic stress, fear of disease progression, and fear of disclosing one's HIV status to others. [5] Understanding these mechanisms is essential for an integrated approach to the patient, combining both medical and psychosocial aspects.

Taking into account all of the above aspects, such as the prevalence of mental disorders in PLWH, the impact of disorders on their quality of life and the effectiveness of treatment, it

should be noted that a review of the literature in this area will provide an overview of the latest research and trends in this field.

Depression

Depression is one of the most common mood disorders, affecting 5.7% of the global population according to the WHO [6]. Its main symptoms include low mood, decreased energy, loss of interest, reduced concentration, and rapid fatigue [7]. The global prevalence of depression in PLWH is estimated at 31%, making it the most common mental illness in PLWH [8]. For this reason, understanding the factors and mechanisms leading to its development in this group of patients is essential to improving their well-being. The development of depression depends primarily on biological and psychosocial factors.

The exact cause of depression is unknown, but there are many theories on the subject. The most popular ones include dysregulation of the hypothalamic–pituitary–adrenal (HPA) or hypothalamic–pituitary–gonadal (HPG) axes, serotonergic transmission disorders, and inflammatory response [9]. There are theories that link the higher incidence of depression in PLWH to an increase in the inflammatory response caused by HIV and its effect on the nervous system. It has been shown that depression is associated with increased concentrations of inflammatory cytokines such as IL-1, IL-6, CRP, and TNF-alpha, which are predictors of depression [10]. Many studies have shown a link between HIV infection, inflammatory response, and the development of depression, but data on this subject are quite scarce and this is definitely an issue that requires more detailed research and observation [11].

In HIV infection, psychosocial factors, particularly internalized stigma, play a key role in the development of depression. Individuals who experience stigmatization are more likely to develop depressive symptoms, and the fear of HIV-status disclosure further exacerbates stress and depression [12]. It has also been shown that symptoms of depression resulting from internalized stigma reduce ART adherence, which means that patients with depression are less likely to achieve viral suppression than patients without depression [13].
The above data indicate the validity of early screening for depression in PLWH.

Posttraumatic stress disorder (PTSD)

Posttraumatic stress disorder (PTSD) is the result of traumatic experiences that leave deep scars on patients' psyches. The prevalence of this disorder in the general population worldwide is 3.9% [14]. However, the estimated prevalence of PTSD among PLWH is much higher, reaching as much as 28% worldwide. It is worth mentioning that the diagnosis of HIV itself and the emotions associated with receiving it can lead to the development of PTSD, as these events fall under criterion A according to the DSM-5 guidelines. Criterion A states that PTSD can develop in people who have experienced a situation in which they feared for their life or health, and a life-long HIV diagnosis can definitely be such a situation [15]. The main symptoms of PTSD include constantly reliving traumatic experiences, avoiding situations that remind them of these experiences, and feeling unsafe.

It is important to detect and treat PTSD, as it has been proven to reduce ART adherence, lower patients' quality of life, and exacerbate symptoms of depression and anxiety. One hypothesis attempting to explain the link between reduced adherence and PTSD is avoidance, which is one of the main symptoms of PTSD. Regular medication reminds patients of their diagnosis and the fear of death. For this reason, they intentionally avoid taking their medication in order to ward off the symptoms of PTSD [16].

Anxiety

Anxiety disorders affect 4.4% of the global population and are characterized by persistent fear and tension, as well as somatic issues, including nausea, increased sweating, and abdominal pains [17]. Anxiety disorders affect 20-40% of PLWH and reduce ART adherence, leading to a delay in viral suppression [18].

It has been proven that the reasons for the higher prevalence of anxiety in PLWH compared to the general population are numerous neurological and immunological disorders. PLWH experience disturbances in the regulation of the hypothalamic pituitary-adrenal (HPA) axis. This axis is also dysregulated in patients with anxiety, so it is predicted that the coexistence of HIV infection and anxiety causes chronic inflammation and axis dysregulation [19].

Substance use disorder (SUD)

Substance abuse is another problem among PLWH. Epidemiological studies indicate an exceptionally high prevalence of substance use disorders (SUD). It has been shown that approximately 48% of PLWH in care centers in the United States meet the diagnostic criteria for at least one SUD, which is a significantly higher percentage than in the general population. The most common substances to which PLWH are addicted include marijuana (31%), alcohol (19%), methamphetamine (13%), cocaine (11%), and opioids (4%). As many as 20% of the study population showed signs of polypharmacy, i.e., simultaneous addiction to multiple substances, which is associated with an increased health risk [20].

On the one hand, drug and alcohol abuse increases the risk of HIV infection through high-risk behaviors such as sharing needles and syringes among people who inject drugs and unprotected sex. On the other hand, the presence of HIV infection can lead to increased substance use as a way of coping with psychological stress and depressive symptoms. Internalized HIV-related stigma and experiences of discrimination have been shown to be significantly associated with increased substance use [21, 22].

The clinical consequences of HIV and SUD co-occurrence are multidimensional and serious. First and foremost, substance abuse has a negative impact on adherence to antiretroviral therapy (ART). Studies have shown that patients undergoing opioid substitution therapy are 54% more likely to adhere to ART treatment recommendations and 45% more likely to achieve viral suppression [23]. In turn, people with alcohol use disorder are up to 4-8 times more likely to non-adhere to treatment recommendations compared to moderate drinkers [24]. In addition, some substances have a synergistic neurotoxic effect with HIV – methamphetamine leads to worsening neurocognitive deficits and accelerated neurodegeneration [25].

Contemporary therapeutic approaches emphasize the integration of HIV treatment with harm reduction programs and addiction therapy. Needle and syringe exchange programs and opioid substitution therapy (methadone, buprenorphine) reduce the risk of HIV transmission by 54%, while improving retention in medical care and virological outcomes. These strategies are consistent with the recommendations of the World Health Organization and UNAIDS, which advocate a holistic approach to people with HIV who use drugs [26].

Cognitive/neuropsychiatric complications

Neurocognitive disorders are a serious problem in PLWH. Studies have shown that the overall prevalence of HIV-associated neurocognitive disorders (HAND) is approximately 42.6%. The severity of neuropsychiatric disorders varies. Among patients with HAND, 23.5% experience asymptomatic neurocognitive impairment (ANI), 13.3% mild neurocognitive disorder (MND), while 5% of patients are diagnosed with HIV-associated dementia (HAD), which represents the most advanced form of the disorder [27].

A significant role in the pathogenesis of HAND is played by CD4 nadir – the lowest CD4 cell count achieved in the past. Numerous studies have shown a strong association between low CD4 nadir and the risk of neurocognitive disorders. In patients whose CD4 count ever fell below 50 cells/mm^3, approximately 60% showed some degree of neurocognitive impairment, and even among those who always maintained immune function (CD4 above 350 cells/mm^3), the incidence was approximately 50%. This so-called "legacy effect" reflects irreversible brain damage that occurs before the immune system has sufficiently recovered [28].

HAD presents with cognitive, behavioral, and motor symptoms. Cognitive deficits include slowing, memory and concentration issues, as well as reduced information processing. Behavioral symptoms can present as apathy, decreased motivation to undertake everyday tasks, and emotional blunting, whereas motor manifestations commonly consist of tremor and postural instability. It is worth noticing that psychomotor slowing can appear even 1 to 2 years before the onset of HAD and can be considered an early marker of progressive CNS damage [29].

Although effective antiretroviral therapy has improved neurocognitive outcomes, it does not fully eliminate HAND. While the frequency of HAD has declined with treatment advances, milder cognitive disturbances persist among individuals with controlled viral loads. Early initiation of ART, prior to a significant decline in CD4 count, and maintenance of optimal therapeutic adherence are key strategies in preventing HAND. Starting ART early, maintaining strong adherence, and including neuropsychological monitoring in HIV care can help detect HAND sooner and support better health outcomes [30].

Discusion

The available literature indicates that the prevalence of mental disorders among PLWH is higher than in general population. Depression remains the most common disorder (31%), and a significant number of patients experience concurrent PTSD (28%) and anxiety disorders (20-40%). Substance use disorders (SUD) affect an estimated 40 and 74% of patients, while neurocognitive disorders (HAND) are diagnosed in 45% of PLWH. Psychiatric disorders frequently overlap, with about 82% patients diagnosed with depression also presenting symptoms of another condition, such as dysthymia or anxiety. The coexistence of multiple factors can exacerbate clinical outcomes and complicate treatment [31].

The co-occurrence of mental disorders in PLWH results from many biological and psychosocial mechanisms that reinforce each other. At the biological level, HIV penetrates the central nervous system and leads to chronic neuroinflammation mediated by cytokines such as IL-6 and TNF-α. These neuroinflammatory cascades are associated with depression in both people with HIV and the general population, but appear to be particularly severe in PLWH. In addition, HIV reduces dopamine concentrations and leads to neurotoxicity, which directly contributes to symptoms of depression and cognitive impairment. Impairments in HPA axis function, observed in both HIV and anxiety disorders, may explain the higher prevalence of co-occurrence of these two conditions. On the other hand, psychosocial factors—stigmatization, discrimination, fear of disclosing HIV status, and loss of social ties—are powerful risk factors for deterioration of mental health [32].

Most mental disorders in PLWH remain undiagnosed, thus early psychiatric screening is crucial. It has been reported that screening programs face significant challenges, such as a lack of included time for psychiatric consultations, inadequate staff preparation, and a lack of specialized diagnostic tools. The main psychiatric therapies that have been registered as effective are harm reduction programs, opioid substitution therapy, and cognitive behavioral therapy (CBT) [33].

Conclusion

Mental disorders in patients living with HIV are a serious public health problem, which is much more prevalent in this population than in the general population and has a significant negative

impact on the course of the disease, adherence to antiretroviral therapy, and the overall well-being of patients. Both biological and psychosocial factors cause the coexistence of HIV and mental health disorders. Viral damage to neurons and neuroinflammation are vast biological contributions, while psychosocial factors, such as internalized stigma and trauma caused by the diagnosis, further increase the vulnerability. Treating mental disorders in PLWH, including medication, psychotherapy, and supportive care, improves ART adherence and increases viral suppression. Additionally, HIV care programs should promote early mental health screening and reduce barriers that limit access to care.

DISCLOSURES

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