Modern American Journal of Medical and Health Sciences
ISSN (E): 3067-803X
Volume 01, Issue 08, November, 2025
Website: usajournals.org

A MODERN LITERATURE REVIEW OF THE PROBLEM OF HIV ENCEPHALOPATHY

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Abstract
This article provides an overview of current concepts of HIV-associated encephalopathy and HIV-associated dementia in the context of the spectrum of HIV-associated neurocognitive disorders (HAND). Epidemiological trends in the era of combination antiretroviral therapy are considered, and a shift from the classical AIDS- dementia complex to the prevalence of mild and moderate cognitive impairment is shown. Key mechanisms of neuropathogenesis are analyzed in detail, including early involvement of the central nervous system, the role of chronic neuroinflammation, blood-brain barrier dysfunction, viral proteins, and concomitant vascular and neurodegenerative pathology. The clinical features of HIV-associated encephalopathy and HIV-associated dementia, and current approaches to diagnostics using neuropsychological testing, neuroimaging, and biomarkers are discussed. Particular attention is paid to the impact of antiretroviral therapy, including integrase inhibitor-based regimens, as well as unresolved issues of adjuvant Neuroprotective treatment. The importance of early screening for cognitive impairment, an interdisciplinary approach, and the development of multimodal diagnostic models integrating clinical, neuroimaging, and laboratory data is emphasized.

Keywords: HIV encephalopathy; HIV-associated dementia; HIV-associated neurocognitive disorders (HAND); neuroinflammation; antiretroviral therapy; biomarkers; neuroimaging; cognitive impairment.

Introductioon

In recent decades, HIV encephalopathy and HIV-associated dementia have been considered in the broader context of HIV-associated neurocognitive disorders

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(HIV-AND). neurocognitive The introduction of combination antiretroviral therapy (ART) has radically reduced the incidence of classic AIDS- dementia complex, but has not completely eliminated cognitive pathology: the spectrum has shifted toward milder, but chronic forms of impairment that significantly impact quality of life, social functioning, and prognosis for patients.

Historically, HIV encephalopathy was described as a subacute progressive brain lesion with the development of dementia, motor, and behavioral disorders in patients in the terminal stages of AIDS. The term "AIDS dementia complex" emphasized the generalized, diffuse nature of the white matter and cerebral cortex damage. With the introduction of ART, severe forms of dementia have become significantly less common, but accumulating data have demonstrated a wide gradation of cognitive impairment—from subclinical to severe—even in the presence of a full virological response. This led to the development of the Franciscan (Frascati) criteria, which distinguish three main categories: asymptomatic neurocognitive impairment (ANI), mild neurocognitive disorder (MND) and HIV-associated dementia (HAD).

Epidemiological studies in recent years indicate that HIV-associated cognitive impairments remain extremely common. A meta-analysis of 49 studies conducted in various regions of the world demonstrated that the overall prevalence of HIV-associated cognitive impairment is approximately 46%, with a very wide range of estimates (14–88%) depending on the methodology, population, and diagnostic criteria. Moreover, severe dementia associated with ART has become rare, while ANI and MND are prevalent. In countries with limited resources, late diagnosis of HIV infection, and limited access to ART, severe forms of HIV encephalopathy remain more common, highlighting the importance of social and organizational factors.

Current understanding of the pathogenesis of HIV encephalopathy and dementia is based on the concept of early and persistent involvement of the central nervous system (CNS) in the infectious process. Already during the primary HIV infection phase, the virus penetrates the blood-brain barrier (BBB), primarily via a "Trojan horse"—infected monocytes and T cells. Stable viral reservoirs form in the CNS, including microglia , perivascular macrophages, and astroglia . Neurons are

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typically not directly infected but are exposed to proinflammatory mediators and viral proteins (Tat , gp120, Nef , etc.), which trigger neurotoxic cascades .

A key role is assigned to the chronic neuroinflammatory response. Immune activation, increased monocyte influx through the disrupted blood-brain barrier, increased expression of cytokines (TNF-α, IL-1β, IL-6, IFN-γ), chemokines (e.g., CXCL10, CCL2), and oxidative stress lead to dysregulation of synaptic transmission, disruption of glutamate homeostasis, and ultimately to apoptosis or functional "silence" of neurons. It has been shown that even in the presence of systemic viral suppression, so-called "CSF escape "—isolated HIV replication in the central nervous system with independent dynamics, accompanied by increased markers of neuronal and glial damage—can persist in the blood and cerebrospinal fluid.

An important topic in recent years has been the comparability of the pathogenesis of HIV-associated dementia with neurodegenerative diseases, primarily Alzheimer's disease. Studies have shown the accumulation of β-amyloid, abnormal patterns of phosphorylated tau, and changes in cerebrospinal fluid biomarkers (Aβ42, total and phosphorylated tau) in some patients with long-term HIV infection and cognitive symptoms. Based on this, the term " Alzheimer's-like dementia in HIV" has been proposed. disease-like dementia , ADLD in HIV). However, the boundary between classical HIV-associated dementia and ADLD remains blurred, and morphological changes are often mixed (neuroinflammation , vascular changes, neurodegeneration).

The contribution of vascular factors—hypertension, diabetes, dyslipidemia, and substance use—to the development of the "vascular cognitive phenotype" in HIV is also being discussed. New data point to a combination of HIV-mediated neuroinflammatory pathology and microvascular lesions, which creates a unique form of vascular cognitive dysfunction associated with HIV infection.

The clinical presentation of HIV-associated encephalopathy and dementia is varied. Classic HAD is characterized by subacutely progressive attention deficits, mental slowing, and decline in executive functions and memory, accompanied by apathy, depression, and irritability. As the disease progresses, severe gait disturbances, pyramidal symptoms, dysarthria, and sometimes extrapyramidal

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disorders may develop. In modern settings, milder forms are more common: patients complain of "brain fog," forgetfulness, difficulty multitasking, decreased reading speed, and difficulty performing tasks requiring concentration. These symptoms are often masked by depression, anxiety disorders, medical comorbidities , and medication side effects.

Current diagnostic approaches to HIV-associated dementia and HIV-associated encephalopathy rely on a combination of neuropsychological assessment, neuroimaging, and laboratory biomarkers. The Franciscan criteria require documented impairment in at least two cognitive domains (attention/processing speed, learning and memory, executive functions, motor skills, and speech) with an assessment of the impact on daily functioning. Short scales (IHDS, MoCA , BNCE, etc.) are widely used for screening; however, their sensitivity and specificity depend on the cultural and educational context. Therefore, recent studies have actively discussed the psychometric properties of these instruments and the need for adaptation to specific populations.

Neuroimaging has expanded our understanding of HIV-associated encephalopathy far beyond mere cerebral atrophy. Structural MRI and diffusion tensor imaging studies reveal volumetric loss in the frontal and parietal regions, basal ganglia, and hippocampus, as well as diffuse white matter lesions that correlate with cognitive impairment. Resting-state functional MRI (rs-fMRI) demonstrates changes in the default mode, frontoparietal , and limbic networks in HIV patients, even in the absence of clinically evident cognitive symptoms. Recent reviews actively explore the use of connectomics —the analysis of brain networks based on graph theory—to identify specific patterns of neurodegeneration in HIV-associated encephalopathy. These network biomarkers are expected to be used for early diagnosis and monitoring of treatment effectiveness.

Particular attention is paid to biomarkers of neuronal and glial damage. Neurofilament light chain (NfL) in blood and cerebrospinal fluid (CSF) is considered one of the most sensitive markers of axonal damage in HIV-AD; its concentration is elevated in patients with cognitive impairment and decreases with effective ART. Glial fibrillary acidic protein (GFAP) reflects astrocytic

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activation, and changes in its levels have been described in both primary HIV infection and chronic disease. In addition, various cytokines and chemokines (e.g., IL-6, CXCL10, CCL2) are being studied as indicators of neuroinflammation , as well as CSF markers of amyloidogenesis and tau pathology, which link HIV-associated dementia to Alzheimer's disease. Current reviews emphasize that an optimal panel of biomarkers suitable for routine clinical practice has not yet been formed, but NfL and some markers of monocyte activation are already actively used in research protocols.

The introduction of combination ART has led to a dramatic reduction in the incidence of severe HIV encephalopathy and dementia, but has not eliminated the problem of cognitive impairment. Studies show that, despite complete virological control, some patients retain viral replication in the CNS and markers of chronic inflammation in the plasma, while cognitive impairment persists or only partially regresses. The concept of "CNS penetration" The cost- effectiveness (CPE) index, which assesses the ability of specific ART regimens to penetrate the blood-brain barrier, has long been considered a promising tool for optimizing therapy. However, large studies have yielded mixed results: higher CPE scores have sometimes been associated with better CSF virological suppression, but not necessarily with better cognitive outcomes, and in some studies, even with an increased risk of neurotoxicity .

However, modern regimens based on integrase inhibitors, particularly dolutegravir , demonstrate a favorable impact on cognitive function. Prospective data indicate improvement or stabilization of cognitive performance within a few months of initiating dolutegravir -containing ART in previously untreated patients. This is explained by both high virological efficacy and good tolerability, as well as a potentially more beneficial effect on neuroinflammation compared to previous-generation drugs.

The question of additional (adjuvant) therapeutic strategies remains open. Anti-inflammatory and neuroprotective agents, microglia modulators , antioxidants, and drugs that affect glutamatergic transmission and neurotrophic factors are being explored. However, most clinical trials to date are either pilot studies or have not demonstrated a clinically significant effect. The strongest evidence base

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currently supports optimization of ART itself, its early initiation (including during acute HIV infection), and the correction of somatic and psychiatric comorbidities. The social and behavioral consequences of HIV-associated dementia and milder forms of HIV-associated dementia are becoming increasingly apparent as people living with HIV live longer. A systematic review found that HIV-associated cognitive impairment is directly associated with decreased treatment adherence, reduced quality of life, disruption of daily activities, and an increased risk of frailty . Some studies highlight the impact of cognitive impairment on employment, financial management, the risk of motor vehicle accidents, and medication errors. Thus, HIV-associated encephalopathy and dementia are moving beyond a purely neurological problem and are becoming an important aspect of general HIV medicine and public health.

In recent years, the early, acute phase of HIV infection has been actively studied as a critical period for the development of future neurocognitive outcomes. Reviews on the neuropathogenesis of acute HIV infection demonstrate that rapid CNS involvement occurs within the first weeks after infection, including increased CSF viral load, elevated NfL and GFAP levels, microglial activation , and disruption of the blood-brain barrier (BBB). Early initiation of ART at this stage can significantly reduce the extent of damage and likely decrease the risk of subsequent HIV-ANR development, although the long-term effects of such strategies have not yet been fully studied.

At the intersection of HIV-associated cognitive impairment and aging, a new area of research is emerging: " neuroHIV in the elderly." The combination of chronic HIV infection, concomitant cardiovascular and metabolic risk factors, and possible AD-like pathology creates a unique profile of cognitive impairment, intertwining elements of classic HIV dementia, vascular cognitive dysfunction, and Alzheimer's disease. This raises serious questions about the choice of diagnostic algorithms (including the use of specific CSF and PET biomarkers), as well as the individualization of therapeutic approaches based on age and comorbidity .

The issue of screening and monitoring HIV-AD in real-world clinical practice deserves special mention. Reviews highlight that despite the availability of

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recommended algorithms, routine cognitive screening is far from always performed, especially in resource-limited settings. This leads to late diagnosis of HIV-associated dementia and the missed diagnosis of mild forms that, nevertheless, significantly impact patient functioning. Current studies suggest integrating short, validated screening scales, adapted to language and culture, into standard HIV clinics, and referring patients for more in-depth neuropsychological assessment and neuroimaging if abnormalities are detected.

Finally, an important area is the search for multimodal models that integrate clinical data, neuropsychological testing results, neuroimaging, and biomarkers. It is expected that such models will allow for better risk stratification of patients, prediction of the dynamics of cognitive impairment, and individualization of therapy. Connectomic studies, advanced rs-fMRI and structural MRI analyses, as well as omics approaches (transcriptomics , proteomics, metabolomics) are already being used to formulate complex biological signatures of HIV-ANR.

Conclusions

Thus, the current literature presents HIV encephalopathy and HIV-associated dementia as part of a complex and heterogeneous spectrum of HIV-associated neurocognitive disorders. A decrease in the incidence of severe forms of dementia in the era of highly active ART is combined with a high prevalence of mild to moderate cognitive impairment associated with persistent Neuroinflammatory activity, incomplete viral suppression in the central nervous system, the impact of comorbid vascular and metabolic factors, and, in the elderly, neurodegenerative processes. Modern research, including advanced neuroimaging, the development of sensitive biomarkers (primarily NfL , GFAP, and monocyte activation markers), analysis of the acute phase of HIV infection, and the evaluation of new ART regimens, are gradually clarifying the pathogenesis and opening the door to earlier diagnosis and targeted therapy. At the same time, it remains clear that effective prevention and treatment of HIV encephalopathy and dementia requires a multidisciplinary approach that combines the efforts of infectious disease specialists, neurologists, psychiatrists, neuropsychologists, and public health specialists, as well as systematic

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consideration of cognitive status in the daily clinical practice of working with people living with HIV.

References

1. Sarvinoz, T., & Muzaffar, Z. (2022). Rehabilitation for childhood cerebral palsy. *Uzbek Scholar Journal*, *6*, 97-101.
2. Nabievna, M. Y., & Muzaffar, Z. (2023). Modern View on the Pathogenesis of Hiv Encephalopathy.
3. Sarvinoz, T., & Muzaffar, Z. (2022). Rehabilitation aspects of water therapy in modern medicine. *Uzbek Scholar Journal*, *6*, 102-106.
4. Nabievna, M. Y., & Muzaffar, Z. (2022). Literatural review of the relevance of the problem of neurosaids. *Modern Journal of Social Sciences and Humanities*, *4*, 558-561.
5. Mukhammadjonov, O. Zokirov M. (2022). Cognitive impairments in patients with HIV-associated encephalopathy. *Central Asian Journal of Medical and Natural Science*, *3*(2), 401-405.
6. Зокиров, М.М., Мухаммаджонов, О. (2022). Когнитивные нарушения у пациентов с болезнью Паркинсона и оптимизация ее лечения.
7. Зокиров, М., & Туланбоева, С. (2022). Когнитивные нарушений у пациентов с ВИЧ–ассоциированной энцефалопатией. *Barqarorlik va yetakchi tadqiqotlar onlayn ilmiy jurnali*, 68-73.
8. Зокиров, М., & Мухаммаджонов, О. (2022). Особенности развития тревожных и депрессивных расстройств при заболеваниях, сопровождающихся хроническим болевым синдромом. *Barqarorlik va yetakchi tadqiqotlar onlayn ilmiy jurnali*, 841-844.
9. Muzaffar, Z., & Okilbeck, M. (2022). Dementia and arterial hypertension. *Modern Journal of Social Sciences and Humanities*, *4*, 19-23.
10. Muzaffar, Z. (2022). HIV Encephalopathy and its Pathogenetic Aspects. *European Multidisciplinary Journal of Modern Science*, *4*, 843-846.
11. Muzaffar, Z. (2022). Literature reviews on nervous system damage during hiv infection. *Barqarorlik va yetakchi tadqiqotlar onlayn ilmiy jurnali*, *2*(9), 141-147.

Modern American Journal of Medical and Health Sciences
ISSN (E): 3067-803X
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Website: usajournals.org

12. Зокиров, М., & Мухаммаджонов, О. (2022). Вич энцефалопатия и его патогенетические аспекты. *Barqarorlik va yetakchi tadqiqotlar onlayn ilmiy jurnali*, 855-858.
13. Зокиров, М. М., Рустамова, И. К., Касимова, С. А., & Кучкарова, О. Б. (2019). Жарохатдан кейинги талвасада кечки нейровизуализацион ўзгаришлар. In *Современная медицина: новые подходы и актуальные исследования* (pp. 56-60).
14. Нессипхан, Б., Шамих Аль-Саеди, Х.Ф., Джассим Аль-сарай, М., Хамид Джасим, Х., Саттар, Р., Али Ахмед, Б., ... и Музаффар, З. (2023). Применение наночастиц оксида железа в качестве усилителей контрастности МРТ: исследование на кроликах. *Журнал наноструктур* , *13* (3), 769-776.
15. Zokiriv, M. (2021). Correction of cognitive impairments in patients with HIV-associated encephalopathy. *J. Theor. Appl. Sci*, *7*, 62-66.
16. Muzaffar, Z. (2022). Psychological State in Patients with HIV Infection. *Amaliy va tibbiyot fanlari ilmiy jurnali*, *1*(6), 52-56.
17. Zokirov, M. M., & Madjidova, Y. N. (2020). Correction Of Cognitive Disorder In Patients With HIV-Associated Encephalopathy. *The American Journal of Medical Sciences and Pharmaceutical Research*, *2*(07), 117-122.
18. Зокиров, М., & Мадмаров, Д. (2022). Корреляция ЭЭГ картины головного мозга и когнтитивного статуса у пациентов с эпилепсией. *Theoretical aspects in the formation of pedagogical sciences*, *1*(5), 227-230.
19. Жахонкуловна С.М., Камоловна Г.Б., Зокиров М., Таджимуратовна Б.У., Юмашев А., Шичьях Р., ..., Ишанкулов А. (2025). Электрохимические биосенсоры для раннего выявления болезни Альцгеймера. *Клиника Химика Акта* , 120278.
20. Muzaffar, Z., & Zarifa, Z. (2023). Yosh bemorlarda gemorragik insultning klinik holatlari. *Psixologiya va sotsiologiya ilmiy jurnali*, *1*(1), 29-31.
21. Zokirov, M. (2023). Features of cognitive impairment in patients with HIV encephalopathy. In *Academic International Conference on Multi-Disciplinary Studies and Education* (Vol. 1, No. 9, pp. 34-36).

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22. Muhammadjonov, o., & Zokirov, m. 2-toifa qandli diabet bilan og'rigan bemorlarda yurak-qon tomir kasalliklarining xavf omillarining tarqalishi. *Студенческий вестник Учредители: Общество с ограниченной ответственностью" Интернаука"*, 53-54.
23. Zokirov, M. M. (2025). Characteristics of post-stroke depression in recurrent ischemic stroke. *Журнал гуманитарных и естественных наук*, (24), 23-27.
24. Muzaffar, Z., & Shirin, D. (2024). Damage to the nervous system due to HIV. *Eurasian Journal of Technology and Innovation*, *2*(7), 39-47.
25. Madjidova, Y., & Zokirov, M. (2024). Cognitive disorders in HIV encephalopathy. *Science and innovation*, *3*(D5), 375-381.