Int. J. Curr. Res. Med. Sci. (2026). 12(1): 22-29

International Journal of Current Research in Medical Sciences

ISSN: 3107-3743 (Print), ISSN: 2454-5716 (Online)
(A Peer Reviewed, Indexed and Open Access Journal)
www.ijcrims.com

Review Article

Volume 12, Issue 1 -2026

DOI: http://dx.doi.org/10.22192/ijcrms.2026.12.01.003

Cytokine Release Syndrome in HIV Patients Receiving Antiretroviral and Immunomodulatory Therapies: Immunopathogenesis, Clinical Features, and Management

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Abstract

Cytokine Release Syndrome (CRS) is a systemic hyperinflammatory condition caused by excessive cytokine production and immune activation. In people living with HIV, CRS can occur during initiation of antiretroviral therapy (ART), immune reconstitution, or administration of immunomodulatory therapies for co-infections, HIV-associated malignancies, or experimental interventions. The pathogenesis involves chronic immune activation, microbial translocation, dysregulated T-cell and monocyte responses, and abrupt immune restoration, which collectively amplify systemic inflammation. Clinically, CRS ranges from mild fever and fatigue to severe multi-organ dysfunction, often mimicking sepsis or immune reconstitution inflammatory syndrome (IRIS). Management focuses on early recognition, supportive care, careful timing of ART, treatment of underlying triggers, and judicious use of immunosuppressive agents such as corticosteroids, with targeted cytokine inhibitors under investigation. Understanding CRS in this context is essential for improving patient outcomes and guiding safe implementation of immune-modulating therapies in HIV.

Keywords: Cytokine Release Syndrome, HIV, Antiretroviral Therapy, Immune Reconstitution Inflammatory Syndrome, Immunomodulatory Therapy

Introduction

Human Immunodeficiency Virus (HIV) infection is not only characterized by progressive depletion of $CD4^+$ T cells and immunodeficiency but also by persistent immune activation and systemic inflammation [1-2]. Even in the era of effective antiretroviral therapy (ART), low-level viral replication, microbial translocation, and immune dysregulation sustain chronic inflammatory states that predispose individuals to exaggerated immune responses. Within this context, Cytokine Release Syndrome (CRS), a severe hyperinflammatory condition driven by excessive cytokine production, has emerged as an important but underrecognized complication in HIV-infected patients receiving ART or immunomodulatory therapies [3-4].CRS in HIV-infected individuals can occur in multiple clinical scenarios. Initiation of ART in severely immunosuppressed patients may trigger immune reconstitution inflammatory syndrome (IRIS), which closely resembles CRS due to rapid restoration of pathogen-specific immune responses and sudden surges of pro-inflammatory cytokines [5-6]. Additionally, the use of immunomodulatory agents—such as checkpoint inhibitors, cytokine therapies, or biologics administered for HIV-associated malignancies or experimental interventions—can further exacerbate inflammatory pathways, increasing the risk of CRS. Co-infections and HIV-associated opportunistic infections serve as additional triggers, compounding the risk in vulnerable patients [7-8].

The immunopathogenesis of CRS in this setting is complex and multifactorial. Persistent T-cell activation, monocyte and macrophage hyperresponsiveness, loss of regulatory immune control, and endothelial dysfunction converge to amplify cytokine-mediated inflammation. Microbial translocation from the damaged gut mucosa and elevated pro-inflammatory cytokines such as interleukin-6 (IL-6), tumor necrosis factor-alpha (TNF-α), and interferon-gamma (IFN-γ) further prime the immune system for hyperactivation. These mechanisms create a delicate balance in which therapeutic interventions intended to restore immune function or target malignancy may inadvertently trigger systemic inflammatory cascades [9-10].Clinically, CRS presents along a spectrum ranging from mild, nonspecific symptoms such as fever, malaise, and myalgia, to life-threatening multi-organ dysfunction involving the cardiovascular, pulmonary, renal, hepatic, and central nervous systems. Its nonspecific presentation and overlap with sepsis, IRIS, opportunistic infections, and drug reactions complicate timely recognition, making early identification and intervention a critical challenge.

Immunopathogenesis of Cytokine Release Syndrome in HIV Patients Receiving ART and Immunomodulatory Therapies

The immunopathogenesis of Cytokine Release Syndrome (CRS) in HIV-infected patients receiving antiretroviral therapy (ART) and immunomodulatory interventions is complex and multifactorial, reflecting the interplay between chronic viral-induced immune dysregulation and therapy-induced immune activation. HIV infection establishes a persistent inflammatory milieu characterized by continuous T-cell and monocyte activation, microbial translocation, and impaired regulatory mechanisms, which collectively prime the host immune system for exaggerated cytokine responses [11-12].Early in HIV infection, depletion of $CD4^+$ T cells in the gut-associated lymphoid tissue disrupts mucosal barrier integrity, permitting translocation of bacterial products such as lipopolysaccharides into systemic circulation. These microbial components stimulate innate immune cells, including monocytes, macrophages, and dendritic cells, through pattern recognition receptors like Toll-like receptors, leading to sustained production of pro-inflammatory cytokines, including interleukin-6 (IL-6), tumor necrosis factor-alpha (TNF-α), and interferon-gamma (IFN-γ). Chronic exposure to these cytokines establishes a state of immune hyperresponsiveness that heightens susceptibility to CRS [13-14].

In patients initiating ART, particularly those with advanced immunosuppression, rapid immune

reconstitution can trigger immune reconstitution inflammatory syndrome (IRIS), a phenomenon closely resembling CRS. The abrupt restoration of pathogen-specific T-cell responses and enhanced cytokine production during IRIS can escalate into systemic hyperinflammation, manifesting as fever, organ dysfunction, and vascular instability. ART-mediated immune recovery, while beneficial for long-term viral suppression, can therefore paradoxically precipitate CRS in susceptible individuals [15-16].The addition of immunomodulatory therapies—including checkpoint inhibitors, cytokine-based therapies, or biologics used to treat HIV-associated malignancies or opportunistic infections—can further amplify this hyperinflammatory state. These interventions enhance T-cell activation or innate immune responsiveness, potentially overwhelming existing regulatory mechanisms and triggering massive cytokine release. Monocytes and macrophages act as central amplifiers, releasing large quantities of IL-6, TNF-α, and IL-1β, which drive endothelial activation, capillary leak, hypotension, and multi-organ dysfunction. Dysregulated adaptive immunity, including exhausted or overactivated $CD4^+$ and $CD8^+$ T cells and impaired regulatory T-cell function, contributes to uncontrolled inflammation and prevents adequate restraint of the cytokine cascade [17-18].Endothelial dysfunction and vascular permeability serve as critical downstream mediators of organ injury in CRS. Excessive cytokine signaling disrupts endothelial integrity, leading to hypotension, tissue edema, and compromised organ perfusion. This vascular involvement links the immunopathogenesis of CRS to the observed clinical manifestations of multi-organ dysfunction in HIV patients undergoing ART or immunomodulatory therapy.

Clinical Manifestations of Cytokine Release Syndrome in HIV Patients Receiving ART and Immunomodulatory Therapies

Cytokine Release Syndrome (CRS) in HIV-infected patients receiving antiretroviral therapy (ART) or immunomodulatory interventions presents with a broad and often nonspecific spectrum of clinical features, reflecting systemic hyperinflammation. The manifestations range from mild constitutional symptoms to severe multi-organ dysfunction, making recognition particularly challenging in the context of HIV, where fever, fatigue, and malaise may already be common due to underlying infection or immune dysregulation [19-20].Early-stage CRS typically presents with systemic inflammatory signs such as persistent fever, chills, fatigue, myalgia, and anorexia. These nonspecific symptoms may develop abruptly or progress gradually and often precede more severe organ involvement. Clinicians must maintain a high index of suspicion, particularly when symptoms occur soon after ART initiation, during immune reconstitution, or following administration of immunomodulatory therapies [21].

Cardiovascular involvement is common in moderate to severe CRS. Patients may exhibit tachycardia, hypotension, and signs of capillary leak, which reflect cytokine-mediated endothelial dysfunction. In severe cases, hypotension may progress to circulatory instability requiring intensive supportive care. Pulmonary manifestations, including dyspnea, hypoxemia, and acute respiratory distress, often arise secondary to increased vascular permeability and pulmonary inflammation. These features may mimic opportunistic infections such as Pneumocystis pneumonia or tuberculosis, complicating differential diagnosis [22-23].Multi-organ involvement extends to hepatic and renal systems. Elevated transaminases, cholestasis, and hepatomegaly may indicate cytokine-driven hepatic inflammation, while acute kidney injury can result from hypotension, endothelial injury, or immune-mediated renal inflammation. In addition, hematologic abnormalities, such as cytopenias or coagulopathy, may be observed, reflecting the systemic impact of inflammatory cytokines on bone marrow and coagulation pathways [24].

Neurological manifestations, though less frequent, are associated with severe CRS and include headache, confusion, altered mental status, and reduced consciousness, reflecting neuroinflammation and blood–brain barrier disruption. These features may be particularly

difficult to distinguish from HIV-associated neurocognitive disorders, CNS infections, or drug-related toxicities [25].The temporal relationship between therapy initiation and symptom onset is a key diagnostic clue. In patients starting ART, CRS-like presentations may overlap with immune reconstitution inflammatory syndrome (IRIS), where sudden restoration of pathogen-specific immunity triggers exaggerated cytokine release. Similarly, the use of immunomodulatory therapies, such as checkpoint inhibitors or biologics, may precipitate abrupt inflammatory responses, leading to CRS [26].

Diagnostic Considerations of Cytokine Release Syndrome in HIV Patients Receiving ART and Immunomodulatory Therapies

Diagnosing Cytokine Release Syndrome (CRS) in HIV-infected patients receiving antiretroviral therapy (ART) or immunomodulatory interventions presents unique challenges due to overlapping clinical features with opportunistic infections, drug reactions, and immune reconstitution inflammatory syndrome (IRIS). The nonspecific presentation—fever, malaise, myalgia, hypotension, and multi-organ involvement—requires careful clinical evaluation to differentiate CRS from other causes of systemic inflammation [27].A high index of suspicion is critical, particularly in patients who develop abrupt or disproportionate inflammatory symptoms following ART initiation, immune restoration, or administration of immunomodulatory therapies. The timing of symptom onset relative to therapy is often a key diagnostic clue: CRS typically emerges within days to weeks of these immune-modulating interventions, while other infections or drug reactions may follow different temporal patterns [28].

Laboratory investigations provide supportive but not definitive evidence of CRS. Elevated inflammatory markers, including C-reactive protein (CRP), ferritin, D-dimer, and lactate dehydrogenase (LDH), reflect systemic immune activation. Cytokine profiling—particularly elevated interleukin-6 (IL-6), interleukin-1β, and tumor necrosis factor-alpha (TNF-α)—can strengthen the diagnosis, though these assays are rarely available in routine clinical practice and lack standardized thresholds for HIV-associated CRS. Hematologic abnormalities such as cytopenias, coagulopathy, and transaminitis may indicate the extent of systemic involvement [29].Exclusion of alternative etiologies is essential. Comprehensive evaluation for bacterial, viral, fungal, and mycobacterial infections is mandatory, as these remain common triggers of fever and organ dysfunction in HIV-infected patients. Drug reactions and adverse effects from ART or immunomodulatory agents must also be considered. In patients recently started on ART, distinguishing CRS from IRIS is particularly challenging, as both conditions share overlapping immunopathogenic mechanisms and clinical manifestations. Serial monitoring of inflammatory markers, organ function, and clinical trajectory can aid in differentiation and in assessing disease severity [29-30].Currently, no standardized diagnostic criteria for CRS exist in HIV-infected populations, and grading systems developed for immunotherapy-associated CRS are not validated in this context. This underscores the need for clinical judgment, careful patient monitoring, and a multidisciplinary approach involving infectious disease specialists, immunologists, and critical care providers.

Therapeutic and Management Implications of Cytokine Release Syndrome in HIV Patients Receiving ART and Immunomodulatory Therapies

The management of Cytokine Release Syndrome (CRS) in HIV-infected patients receiving antiretroviral therapy (ART) or immunomodulatory interventions is complex and must balance suppression of harmful inflammation with preservation of immune function. Unlike CRS associated with immunotherapies in oncology, there are no standardized treatment guidelines specifically for HIV-associated CRS, making individualized clinical decision-making essential [31-32].The cornerstone of management is early recognition and prompt treatment of precipitating factors. Opportunistic infections, co-infections, and HIV-

associated malignancies are common triggers and should be aggressively investigated and treated. Optimization of ART is also critical; in patients not yet on therapy, careful timing of initiation and monitoring are necessary to reduce the risk of immune reconstitution–related hyperinflammation. For patients already on ART, ensuring adherence and viral suppression can help limit ongoing immune activation and mitigate further cytokine surges [33-34].

Supportive care is a fundamental component of therapy. Patients may require close monitoring of vital signs, fluid resuscitation, oxygen supplementation, and intensive care support for cardiovascular or respiratory instability. Multi-organ involvement—particularly renal, hepatic, or neurological—necessitates careful monitoring and early intervention to prevent irreversible damage [35-36].Immunomodulatory therapy plays a central role in patients with severe or progressive CRS. Corticosteroids are the most widely used agents, especially in cases associated with immune reconstitution inflammatory syndrome, due to their ability to broadly suppress cytokine production and reduce systemic inflammation. However, corticosteroid use must be carefully balanced against the increased risk of secondary infections and delayed viral clearance, particularly in severely immunocompromised individuals 37-38].

Targeted cytokine inhibitors, such as interleukin-6 (IL-6) receptor antagonists or interleukin-1 (IL-1) blockers, represent emerging therapeutic options. While evidence from oncology and experimental studies suggests efficacy in controlling hyperinflammatory states, their use in HIV-infected patients remains largely investigational. Considerations include potential immunosuppressive effects, drug–drug interactions with ART, and limited availability in resource-constrained settings [39-41].Multidisciplinary care is essential for optimizing outcomes. Collaboration among infectious disease specialists, immunologists, and critical care teams facilitates comprehensive assessment, early recognition of clinical deterioration, and timely intervention. Serial monitoring of inflammatory markers, organ function, and patient response guides therapy adjustment and tapering of immunosuppressive agents [42-43].

Conclusion

Cytokine Release Syndrome (CRS) in HIV-infected patients receiving antiretroviral therapy (ART) and immunomodulatory interventions represents a significant manifestation of immune dysregulation, arising from the convergence of chronic HIV-driven inflammation, therapy-induced immune restoration, and immune-enhancing treatments. Its clinical presentation is highly variable, ranging from mild systemic symptoms to severe multi-organ dysfunction, often overlapping with opportunistic infections, drug reactions, and immune reconstitution inflammatory syndrome (IRIS).Early recognition of CRS is critical, as timely intervention can prevent progression to life-threatening complications. Management requires a multifaceted approach that includes supportive care, treatment of underlying triggers, careful modulation of ART initiation or continuation, and judicious use of immunosuppressive agents such as corticosteroids. Emerging targeted therapies against key cytokines, such as IL-6 inhibitors, offer promising avenues but remain investigational in this context.Future research should focus on establishing standardized diagnostic criteria, identifying reliable biomarkers, and evaluating targeted therapeutic strategies specific to HIV-associated CRS. Integrating CRS awareness into HIV care frameworks will improve early detection, enable precise risk stratification, and optimize the safe use of immunomodulatory therapies, ultimately enhancing outcomes for people living with HIV.

References

1. Boasso, A., Shearer, G. M., &Chougnet, C. (2009). Immune dysregulation in human immunodeficiency virus infection: know it, fix it, prevent it?.*Journal of internal medicine*, *265*(1), 78–96. https://doi.org/10.1111/j.1365-2796.2008.02043.x

2. Klatt, N. R., Chomont, N., Douek, D. C., &Deeks, S. G. (2013). Immune activation and HIV persistence: implications for curative approaches to HIV infection. *Immunological reviews*, *254*(1), 326–342. https://doi.org/10.1111/imr.12065
3. Obeagu, E. I., Obeagu, G. U., Ede, M. O., Odo, E. O., & Buhari, H. A. (2023). Translation of HIV/AIDS knowledge into behavior change among secondary school adolescents in Uganda: A review. *Medicine*, *102*(49), e36599. https://doi.org/10.1097/MD.0000000000036599
4. Obeagu, E. I., Obeagu, G. U., Ukibe, N. R., &Oyebadejo, S. A. (2024). Anemia, iron, and HIV: decoding the interconnected pathways: A review. *Medicine*, *103*(2), e36937. https://doi.org/10.1097/MD.0000000000036937
5. Li, X., Shao, M., Zeng, X., Qian, P., & Huang, H. (2021). Signaling pathways in the regulation of cytokine release syndrome in human diseases and intervention therapy. *Signal transduction and targeted therapy*, *6*(1), 367. https://doi.org/10.1038/s41392-021-00764-4
6. Panoskaltsis N. (2021). Are all cytokine storms the same?.*Cancer immunology, immunotherapy : CII*, *70*(4), 887–892. https://doi.org/10.1007/s00262-020-02822-2
7. Klatt, N. R., Funderburg, N. T., &Brenchley, J. M. (2013). Microbial translocation, immune activation, and HIV disease. *Trends in microbiology*, *21*(1), 6–13. https://doi.org/10.1016/j.tim.2012.09.001
8. Brenchley, J. M., &Douek, D. C. (2008). The mucosal barrier and immune activation in HIV pathogenesis. *Current opinion in HIV and AIDS*, *3*(3), 356–361. https://doi.org/10.1097/COH.0b013e3282f9ae9c
9. Obeagu, E. I., Obeagu, G. U., Ubosi, N. I., Uzoma, I. C., &Tayrab, E. M. A. (2024). Concurrent management of HIV and malaria: A comprehensive review of strategies to enhance quality of life. *Medicine*, *103*(14), e37649. https://doi.org/10.1097/MD.0000000000037649
10. Wong, C. S., Richards, E. S., Pei, L., &Sereti, I. (2017). Immune reconstitution inflammatory syndrome in HIV infection: taking the bad with the good. *Oral diseases*, *23*(7), 822–827. https://doi.org/10.1111/odi.12606
11. Sharma, S. K., &Soneja, M. (2011). HIV & immune reconstitution inflammatory syndrome (IRIS). *The Indian journal of medical research*, *134*(6), 866–877. https://doi.org/10.4103/0971-5916.92632
12. Catalfamo, M., Le Saout, C., & Lane, H. C. (2012). The role of cytokines in the pathogenesis and treatment of HIV infection. *Cytokine & growth factor reviews*, *23*(4-5), 207–214. https://doi.org/10.1016/j.cytogfr.2012.05.007
13. Plaeger, S. F., Collins, B. S., Musib, R., Deeks, S. G., Read, S., & Embry, A. (2012). Immune activation in the pathogenesis of treated chronic HIV disease: a workshop summary. *AIDS research and human retroviruses*, *28*(5), 469–477. https://doi.org/10.1089/aid.2011.0213
14. Obeagu, E. I., &Obeagu, G. U. (2024). Platelet index ratios in HIV: Emerging biomarkers for immune health and disease management. *Medicine*, *103*(12), e37576. https://doi.org/10.1097/MD.0000000000037576
15. Vidya Vijayan, K. K., Karthigeyan, K. P., Tripathi, S. P., & Hanna, L. E. (2017). Pathophysiology of CD4+ T-Cell Depletion in HIV-1 and HIV-2 Infections. *Frontiers in immunology*, *8*, 580. https://doi.org/10.3389/fimmu.2017.00580
16. Guadalupe, M., Reay, E., Sankaran, S., Prindiville, T., Flamm, J., McNeil, A., & Dandekar, S. (2003). Severe CD4+ T-cell depletion in gut lymphoid tissue during primary human immunodeficiency virus type 1 infection and substantial delay in restoration following highly active antiretroviral therapy. *Journal of virology*, *77*(21), 11708–11717. https://doi.org/10.1128/jvi.77.21.11708-11717.2003
17. Campbell, J. H., Hearps, A. C., Martin, G. E., Williams, K. C., & Crowe, S. M. (2014). The importance of monocytes and macrophages in HIV pathogenesis, treatment, and cure. *AIDS*

(London, England), *28*(15), 2175–2187. https://doi.org/10.1097/QAD.0000000000000408

18. Herskovitz, J., & Gendelman, H. E. (2019). HIV and the Macrophage: From Cell Reservoirs to Drug Delivery to Viral Eradication. *Journal of neuroimmune pharmacology : the official journal of the Society on NeuroImmune Pharmacology*, *14*(1), 52–67. https://doi.org/10.1007/s11481-018-9785-6
19. Obeagu, E. I., Isiko, I., &Obeagu, G. U. (2025). Immunological factors influencing HIV acquisition in infants: A narrative review. *Medicine*, *104*(25), e43039. https://doi.org/10.1097/MD.0000000000043039
20. Wu, Y., Wu, Y., Gao, Z., Yu, W., Zhang, L., & Zhou, F. (2026). Revitalizing T cells: breakthroughs and challenges in overcoming T cell exhaustion. *Signal transduction and targeted therapy*, *11*(1), 2. https://doi.org/10.1038/s41392-025-02327-3
21. Wilson, E. M., &Sereti, I. (2013). Immune restoration after antiretroviral therapy: the pitfalls of hasty or incomplete repairs. *Immunological reviews*, *254*(1), 343–354. https://doi.org/10.1111/imr.12064
22. Anand, A. R., Rachel, G., & Parthasarathy, D. (2018). HIV Proteins and Endothelial Dysfunction: Implications in Cardiovascular Disease. *Frontiers in cardiovascular medicine*, *5*, 185. https://doi.org/10.3389/fcvm.2018.00185
23. Anand AR, Rachel G, Parthasarathy D. HIV Proteins and Endothelial Dysfunction: Implications in Cardiovascular Disease. Front Cardiovasc Med. 2018 Dec 19;5:185. doi: 10.3389/fcvm.2018.00185. PMID: 30619892; PMCID: PMC6305718.
24. Obeagu, E. I., &Obeagu, G. U. (2024). Utilization of immunological ratios in HIV: Implications for monitoring and therapeutic strategies. *Medicine*, *103*(9), e37354. https://doi.org/10.1097/MD.0000000000037354
25. Muthuka, J. K., Jr, Oluoch, K., Wambura, F. M., Nzioki, J. M., &Nabaweesi, R. (2023). HIV and Associated Indicators of COVID-19 Cytokine Release Syndrome: A Meta-Analysis and Meta-Regression. *Cureus*, *15*(2), e34688. https://doi.org/10.7759/cureus.34688
26. Deeks, S. G., Tracy, R., &Douek, D. C. (2013). Systemic effects of inflammation on health during chronic HIV infection. *Immunity*, *39*(4), 633–645. https://doi.org/10.1016/j.immuni.2013.10.001
27. Ebdrup, L., Druey, K. M., Druey, K., &Mogensen, T. H. (2018). Severe capillary leak syndrome with cardiac arrest triggered by influenza virus infection. *BMJ case reports*, *2018*, bcr2018226108. https://doi.org/10.1136/bcr-2018-226108
28. Matthay, M. A., Zemans, R. L., Zimmerman, G. A., Arabi, Y. M., Beitler, J. R., Mercat, A., Herridge, M., Randolph, A. G., & Calfee, C. S. (2019). Acute respiratory distress syndrome. *Nature reviews. Disease primers*, *5*(1), 18. https://doi.org/10.1038/s41572-019-0069-0
29. Swenson, K. E., & Swenson, E. R. (2021). Pathophysiology of Acute Respiratory Distress Syndrome and COVID-19 Lung Injury. *Critical care clinics*, *37*(4), 749–776. https://doi.org/10.1016/j.ccc.2021.05.003
30. Obeagu, E. I., Obeagu, G. U., &Akinleye, C. A. (2024). Unveiling the enigmatic roles of basophils in HIV infection: A narrative review. *Medicine*, *103*(44), e40384. https://doi.org/10.1097/MD.0000000000040384
31. Betrosian, A. P., Agarwal, B., &Douzinas, E. E. (2007). Acute renal dysfunction in liver diseases. *World journal of gastroenterology*, *13*(42), 5552–5559. https://doi.org/10.3748/wjg.v13.i42.5552
32. Mireskandari, Z. S., Haddad, M., Sheybani, F., Bojdi, A., & Moghadam, M. D. (2025). Neurological manifestations in HIV-infected patients: a retrospective cohort study in Northeastern Iran. *Virology journal*, *22*(1), 291. https://doi.org/10.1186/s12985-025-02911-7
33. Arvanitis, P., Tziotis, A., Papadimatos, S., &Farmakiotis, D. (2025). Pathogenesis, Diagnosis, and Management of Cytokine Release Syndrome in Patients with Cancer: Focus on Infectious Disease Considerations. *Current oncology (Toronto, Ont.)*, *32*(4), 198. https://doi.org/10.3390/curroncol32040198

34. Wang, C. X., Letendre, S. L., Hong, S., Andalibi, M., Iudicello, J. E., & Ellis, R. J. (2025). Differential systemic immune-inflammation index levels in people with and without HIV infection. *AIDS (London, England)*, *39*(5), 554–559. https://doi.org/10.1097/QAD.0000000000004088
35. Harrison M. (2015). Erythrocyte sedimentation rate and C-reactive protein. *Australian prescriber*, *38*(3), 93–94. https://doi.org/10.18773/austprescr.2015.034
36. Obeagu, E. I., &Goryacheva, O. G. (2025). Osteomyelitis in HIV pathogenesis, challenges, and therapeutic strategies. *Annals of medicine and surgery (2012)*, *88*(1), 459–469. https://doi.org/10.1097/MS9.0000000000004326
37. Signore, A., Glaudemans, A. W., Galli, F., &Rouzet, F. (2015). Imaging infection and inflammation. *BioMed research international*, *2015*, 615150. https://doi.org/10.1155/2015/615150
38. Lee, D. W., Gardner, R., Porter, D. L., Louis, C. U., Ahmed, N., Jensen, M., Grupp, S. A., & Mackall, C. L. (2014). Current concepts in the diagnosis and management of cytokine release syndrome. *Blood*, *124*(2), 188–195. https://doi.org/10.1182/blood-2014-05-552729
39. Arvanitis, P., Tziotis, A., Papadimatos, S., &Farmakiotis, D. (2025). Pathogenesis, Diagnosis, and Management of Cytokine Release Syndrome in Patients with Cancer: Focus on Infectious Disease Considerations. *Current oncology (Toronto, Ont.)*, *32*(4), 198. https://doi.org/10.3390/curroncol32040198
40. Boozhmehrani, M. J., Hoseinnejad, A., Lesani, S., Afzalzadeh, S., YousefiFard, A., Rezaei-Matehkolaei, A., Maraghi, S., Tavalla, M., TaghizadehArmaki, M., Jafarzadeh, J., &Bastani, M. N. (2025). Comprehensive Management of HIV With Multiple Opportunistic Infections: A Case Report. *Clinical case reports*, *13*(10), e71216. https://doi.org/10.1002/ccr3.71216
41. Athale, J., Busch, L. M., & O'Grady, N. P. (2022). Cytokine Release Syndrome and Sepsis: Analogous Clinical Syndromes with Distinct Causes and Challenges in Management. *Infectious disease clinics of North America*, *36*(4), 735–748. https://doi.org/10.1016/j.idc.2022.07.001
42. Razmi, M., Hashemi, F., Gheytanchi, E., DehghanManshadi, M., Ghods, R., &Madjd, Z. (2020). Immunomodulatory-based therapy as a potential promising treatment strategy against severe COVID-19 patients: A systematic review. *International immunopharmacology*, *88*, 106942. https://doi.org/10.1016/j.intimp.2020.106942
43. Chen, J. J., Zhang, L. N., Hou, H., Xu, L., & Ji, K. (2021). Interleukin-6 signaling blockade treatment for cytokine release syndrome in COVID-19 (Review). *Experimental and therapeutic medicine*, *21*(1), 24. https://doi.org/10.3892/etm.2020.9456

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Subject: Immunopharmacology

Quick Response Code

DOI: 10.22192/ijcrms.2026.12.01.003

How to cite this article:
Emmanuel Ifeanyi Obeagu and Amarachi Suzzy-Martins Ezekwunem. (2026). Cytokine Release Syndrome in HIV Patients Receiving Antiretroviral and Immunomodulatory Therapies: Immunopathogenesis, Clinical Features, and Management. Int. J. Curr. Res. Med. Sci. 12(1): 22-29.
DOI: http://dx.doi.org/10.22192/ijcrms.2026.12.01.003