Int. J. Curr. Res. Med. Sci. (2026). 12(1): 13-21

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.2026.12.01.002

Cytokine Release Syndrome in HIV Infection: Immunopathogenesis, Clinical Features, and Therapeutic and Management Implications

***Emmanuel Ifeanyi Obeagu[1,2] and Amarachi Suzzy-Martins Ezekwunem[3]**

[1]Division of Haematology, Department of Biomedical and Laboratory Science, Africa University, Zimbabwe.

[2]Department of Molecular Medicine and Haematology, School of Pathology, Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, South Africa

[3]Department of Medical Laboratory Sciences, Madonna University, Elele, Rivers State, Nigeria

*Corresponding author: Emmanuel Ifeanyi Obeagu, Department of Biomedical and Laboratory Science, Africa University, Zimbabwe, emmanuelobeagu@yahoo.com,

ORCID: 0000-0002-4538-0161

Abstract

Cytokine Release Syndrome (CRS) is a severe hyperinflammatory condition characterized by excessive and dysregulated cytokine production, leading to systemic immune activation and organ dysfunction. Although most commonly associated with immunotherapies, CRS is increasingly recognized in infectious diseases, including Human Immunodeficiency Virus (HIV) infection. HIV is marked by persistent immune activation, cytokine imbalance, and immune dysregulation, creating a biological milieu conducive to CRS, particularly during acute infection, advanced immunosuppression, opportunistic co-infections, and immune reconstitution following antiretroviral therapy initiation. Key pathogenic mechanisms include chronic T-cell and monocyte activation, microbial translocation, endothelial dysfunction, and impaired immune regulation. Clinically, CRS in HIV ranges from mild inflammatory symptoms to life-threatening multisystem involvement, often mimicking sepsis or immune reconstitution inflammatory syndrome, thereby complicating diagnosis. Management remains largely supportive and trigger-directed, with corticosteroids commonly employed in severe cases, while targeted cytokine therapies remain investigational. Improved understanding of CRS in HIV is essential for early recognition, risk stratification, and development of targeted therapeutic strategies to reduce morbidity and mortality.

Keywords: Cytokine Release Syndrome, HIV Infection, Immune Activation, Hyperinflammation, Immunopathogenesis

Introduction

Human Immunodeficiency Virus (HIV) infection is characterized by profound and persistent immune dysregulation that extends beyond progressive immunodeficiency [1-2]. Even in the era of effective antiretroviral therapy (ART), chronic immune activation and systemic inflammation remain central features of HIV pathogenesis and are strongly linked to disease progression, immune exhaustion, and non-AIDS–related morbidity and mortality. Within this inflammatory landscape, Cytokine Release Syndrome (CRS) has emerged as a clinically relevant but underrecognized complication of HIV infection [3-4].CRS refers to a state of excessive and uncontrolled cytokine production resulting from heightened immune cell activation. It is classically described in association with immunotherapeutic interventions, such as chimeric antigen receptor (CAR) T-cell therapy; however, similar hyperinflammatory syndromes are increasingly reported in infectious diseases. In HIV infection, the continuous interaction between viral replication, host immune responses, and environmental triggers creates conditions that closely resemble the immunopathological processes observed in CRS. Episodes of abrupt cytokine surges may occur during acute HIV seroconversion, advanced untreated disease, initiation of ART, or in the presence of opportunistic infections and HIV-associated malignancies [5-6].

The immunological basis of CRS in HIV is multifactorial. Early disruption of the gut mucosal barrier facilitates microbial translocation, leading to sustained activation of innate immune pathways and excessive production of pro-inflammatory cytokines such as interleukin-6, tumor necrosis factor-alpha, and interferon-gamma. Concurrently, HIV-driven depletion and dysfunction of $CD4^+$ T cells impair immune regulation, while activated monocytes and macrophages serve as major amplifiers of inflammatory signaling. This imbalance between immune activation and immune control predisposes individuals living with HIV to exaggerated inflammatory responses that can escalate into CRS [7-9].Clinically, CRS in HIV presents with a broad and often nonspecific spectrum of manifestations, including fever, hemodynamic instability, and multi-organ dysfunction. These features overlap significantly with sepsis, immune reconstitution inflammatory syndrome (IRIS), and severe opportunistic infections, making diagnosis particularly challenging, especially in resource-limited settings where advanced immunological assays are unavailable. As a result, CRS may be underdiagnosed or misclassified, contributing to delayed or suboptimal management [10-11].Despite growing recognition of inflammation as a key driver of HIV-associated morbidity, CRS has not been systematically integrated into HIV clinical frameworks. A clearer conceptualization of CRS in the context of HIV infection is essential to improve clinical recognition, refine diagnostic approaches, and guide therapeutic decision-making. This narrative review aims to synthesize current evidence on the immunopathogenesis and clinical implications of CRS in HIV infection, highlighting gaps in knowledge and identifying opportunities for future research and targeted intervention.

Immunopathogenesis of Cytokine Release Syndrome in HIV Infection

The immunopathogenesis of Cytokine Release Syndrome (CRS) in HIV infection is rooted in the virus's unique capacity to induce persistent immune activation and disrupt immune regulatory mechanisms. Unlike transient inflammatory responses seen in most acute infections, HIV establishes a chronic state of immune stimulation that primes the host for exaggerated cytokine responses when additional immunological triggers are encountered. This persistent inflammatory environment provides the biological foundation upon which CRS can develop [12-14].Early in HIV infection, massive depletion of $CD4^+$ T cells occurs within the gut-associated lymphoid tissue, leading to breakdown of mucosal integrity. This damage permits translocation of microbial products, such as lipopolysaccharides and bacterial DNA, into the systemic circulation. These microbial products activate innate immune cells through pattern recognition receptors, including Toll-like receptors, resulting in

sustained production of pro-inflammatory cytokines. Interleukin-6, tumor necrosis factor-alpha, interleukin-1β, and type I and II interferons become chronically elevated, creating a state of immune hyperresponsiveness that predisposes to CRS [15-16].

Monocytes and macrophages are central drivers of cytokine amplification in HIV-associated CRS. HIV infection skews these cells toward a pro-inflammatory phenotype, characterized by heightened responsiveness to secondary stimuli. Activated monocytes produce large quantities of interleukin-6 and tumor necrosis factor-alpha, key mediators implicated in vascular permeability, hypotension, and organ dysfunction. In advanced HIV disease, the regulatory mechanisms that normally constrain monocyte activation are impaired, allowing inflammatory cascades to proceed unchecked [17-19].Adaptive immune dysregulation further contributes to CRS pathogenesis. Persistent antigenic stimulation leads to chronic activation and exhaustion of $CD4^+$ and $CD8^+$ T cells. While exhausted T cells display impaired antiviral function, they continue to secrete inflammatory cytokines, particularly interferon-gamma, thereby perpetuating systemic inflammation. Concurrent loss of regulatory T-cell function diminishes immune tolerance and fails to restrain excessive cytokine production, tipping the balance toward hyperinflammation [20].

The initiation of antiretroviral therapy represents a critical immunological turning point in HIV infection. In individuals with advanced immunosuppression, rapid restoration of immune function can trigger immune reconstitution inflammatory syndrome, a clinical entity that shares significant overlap with CRS. The sudden resurgence of pathogen-specific immune responses results in abrupt cytokine surges, driven by reactivated T cells and macrophages responding to residual antigens. This immune reconstitution–associated inflammation can escalate into a CRS-like state, particularly in the presence of opportunistic infections [21].Endothelial activation and dysfunction represent downstream consequences of excessive cytokine release in HIV-associated CRS. Pro-inflammatory cytokines promote endothelial permeability, coagulation abnormalities, and microvascular injury, contributing to hypotension and multi-organ involvement. These vascular changes not only amplify systemic inflammation but also link CRS to the increased cardiovascular and thromboembolic risks observed in people living with HIV [22-24].

Clinical Manifestations of Cytokine Release Syndrome in HIV Infection

The clinical manifestations of Cytokine Release Syndrome (CRS) in HIV infection are diverse, nonspecific, and often overlap with other inflammatory and infectious complications commonly encountered in people living with HIV. This overlap contributes to underrecognition of CRS, particularly in patients with advanced disease, opportunistic infections, or those undergoing immune reconstitution following initiation of antiretroviral therapy [25].CRS in HIV typically presents with constitutional symptoms driven by systemic inflammation. Persistent or high-grade fever is the most frequent early feature, often accompanied by fatigue, malaise, myalgia, and anorexia. These symptoms may appear abruptly or evolve over days and are frequently indistinguishable from acute infections or sepsis. In HIV-infected individuals with chronic immune activation, even minor immunological triggers may precipitate a rapid escalation of symptoms [26].

As CRS progresses, cardiovascular manifestations become prominent. Patients may develop tachycardia, hypotension, and signs of capillary leak, reflecting cytokine-mediated endothelial dysfunction. Hypotension may range from mild to severe and, in advanced cases, can lead to circulatory instability requiring intensive supportive care. These features are particularly concerning in individuals with advanced HIV disease or concurrent infections, where physiological reserves are limited [27].Respiratory involvement is common and may manifest as tachypnea, hypoxemia, or acute lung injury. Elevated cytokine levels promote increased vascular permeability within the pulmonary microcirculation, resulting in

interstitial edema and impaired gas exchange. Clinically, this may mimic pneumonia or acute respiratory distress syndrome, especially in patients with coexisting pulmonary opportunistic infections such as tuberculosis or Pneumocystis pneumonia [28-30].

Hepatic and renal dysfunction are frequently observed in moderate to severe CRS. Hepatic involvement may present with elevated transaminases, cholestasis, or hepatomegaly, reflecting inflammatory injury and altered hepatic perfusion. Renal manifestations range from mild creatinine elevation to acute kidney injury, driven by hypotension, cytokine-induced endothelial damage, and immune-mediated renal inflammation. These organ dysfunctions significantly worsen prognosis if not promptly recognized and managed [31].Neurological manifestations, though less common, represent severe CRS involvement. Patients may exhibit headache, confusion, altered mental status, or reduced consciousness, reflecting neuroinflammation and disruption of the blood–brain barrier. In individuals with HIV, these symptoms pose diagnostic challenges, as they overlap with central nervous system infections and HIV-associated neurocognitive disorders [32].In the context of immune reconstitution inflammatory syndrome, CRS-like manifestations may emerge shortly after initiation of antiretroviral therapy. These presentations are often marked by exaggerated inflammatory responses at sites of previous or occult infections, accompanied by systemic symptoms and organ dysfunction. The temporal relationship with ART initiation serves as a key clinical clue, although definitive distinction between IRIS and CRS remains challenging.

Diagnostic Considerations in Cytokine Release Syndrome Associated with HIV Infection

Diagnosing Cytokine Release Syndrome (CRS) in the context of HIV infection is particularly challenging due to its nonspecific clinical presentation and significant overlap with other common HIV-related conditions. Fever, systemic inflammation, and organ dysfunction—hallmark features of CRS—are also characteristic of sepsis, opportunistic infections, immune reconstitution inflammatory syndrome (IRIS), and HIV-associated malignancies. As a result, CRS in people living with HIV is likely underdiagnosed or misclassified, especially in resource-limited settings [33].A high index of clinical suspicion is essential for diagnosis. CRS should be considered in HIV-infected individuals who present with persistent or rapidly escalating inflammatory symptoms that are disproportionate to identified infectious or structural causes. Temporal patterns provide important diagnostic clues, particularly the onset of symptoms following initiation of antiretroviral therapy, during acute HIV seroconversion, or in the setting of known opportunistic infections or malignancies undergoing treatment [34].

Laboratory evaluation plays a supportive but not definitive role in diagnosis. Elevated inflammatory markers such as C-reactive protein, ferritin, erythrocyte sedimentation rate, and D-dimer are commonly observed and reflect systemic immune activation. Among cytokines, interleukin-6 is frequently elevated and correlates with disease severity in CRS; however, routine cytokine profiling is often unavailable and lacks standardized thresholds in HIV-associated CRS. Cytopenias, transaminitis, coagulopathy, and elevated lactate levels may further support the presence of a hyperinflammatory state [35].Exclusion of alternative diagnoses is a critical component of the diagnostic process. Comprehensive evaluation for bacterial, viral, fungal, and mycobacterial infections is mandatory, as untreated infections remain a leading cause of inflammation and mortality in HIV. Similarly, careful assessment for IRIS is required, particularly in patients recently initiated on ART, as IRIS and CRS share overlapping immunopathological features and clinical manifestations [36].

Imaging and organ-specific investigations may assist in assessing the extent of systemic involvement but are rarely diagnostic of CRS itself. Radiographic findings often reflect secondary inflammatory damage rather than a primary pathological process. In severe cases, trends in inflammatory markers and clinical

deterioration despite appropriate antimicrobial therapy may strengthen the suspicion of CRS [37].Importantly, there are currently no universally accepted diagnostic criteria for CRS in infectious diseases, including HIV. Existing CRS grading systems developed for immunotherapy-associated CRS may provide a conceptual framework but lack validation in HIV populations. This diagnostic gap underscores the need for context-specific criteria that integrate clinical severity, inflammatory biomarkers, and HIV-related factors [38].

Therapeutic and Management Implications of Cytokine Release Syndrome in HIV Infection

The management of Cytokine Release Syndrome (CRS) in HIV infection is complex and requires a nuanced approach that balances control of excessive inflammation with preservation of host immune defense. Unlike immunotherapy-associated CRS, for which standardized treatment algorithms exist, HIV-associated CRS lacks clearly defined management guidelines. Consequently, therapeutic decisions are largely individualized and driven by clinical severity, underlying triggers, and the patient's immunological status [39].The cornerstone of management is prompt identification and treatment of precipitating factors. Opportunistic infections, co-infections, and HIV-associated malignancies frequently act as triggers for CRS and must be aggressively investigated and appropriately treated. Optimization of antiretroviral therapy is equally critical. In patients not yet on ART, initiation of therapy must be carefully timed and monitored, particularly in those with advanced immunosuppression, to minimize the risk of excessive inflammatory responses. In individuals already receiving ART, adherence and virologic suppression should be reassessed to reduce ongoing immune activation [40].

Supportive care remains fundamental in all cases of CRS. Management of fever, maintenance of hemodynamic stability, and monitoring of organ function are essential, particularly in moderate to severe disease. Patients with hypotension, hypoxemia, or evolving organ dysfunction may require intensive care support. Early recognition of clinical deterioration and escalation of care are crucial to improving outcomes [41].Immunomodulatory therapy plays a central role in severe or progressive CRS. Corticosteroids are the most commonly used agents, particularly in CRS associated with immune reconstitution inflammatory syndrome. By broadly suppressing cytokine production and immune activation, corticosteroids can rapidly ameliorate symptoms and prevent further organ damage. However, their use must be carefully weighed against the risk of secondary infections, especially in severely immunocompromised individuals [42].

Targeted cytokine inhibition represents a promising but largely investigational approach in HIV-associated CRS. Therapies aimed at key inflammatory mediators, such as interleukin-6 or interleukin-1, have shown efficacy in other CRS contexts but remain insufficiently studied in people living with HIV. Concerns regarding immunosuppression, drug–drug interactions with ART, and cost limit widespread adoption, particularly in resource-constrained settings. Nevertheless, these agents may offer future therapeutic options for refractory or life-threatening cases [43].Close clinical monitoring is essential throughout the course of CRS management. Serial assessment of inflammatory markers, organ function, and clinical status helps guide treatment decisions and tapering of immunosuppressive therapy. Multidisciplinary collaboration among infectious disease specialists, immunologists, and critical care teams enhances comprehensive care and risk mitigation.

Conclusion

Cytokine Release Syndrome represents an important yet underrecognized manifestation of immune dysregulation in HIV infection. Driven by chronic immune activation, microbial translocation, impaired immune regulation, and abrupt immune restoration, CRS reflects an extreme end of the HIV-associated inflammatory spectrum rather than a distinct pathological entity. Its clinical presentation is heterogeneous and often indistinguishable from sepsis, opportunistic infections, or immune reconstitution

inflammatory syndrome, contributing to diagnostic and therapeutic challenges.Recognition of CRS in people living with HIV has significant clinical implications. Early identification and appropriate management can mitigate progression to severe organ dysfunction and reduce mortality, particularly in individuals with advanced disease or concurrent infections. Current management strategies rely largely on supportive care, treatment of underlying triggers, and cautious use of immunomodulatory therapies, underscoring the absence of standardized, HIV-specific guidelines.

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

Access this Article in Online	
Quick Response Code	Website: www.ijcrims.com Subject: Pathophysiology
DOI: 10.22192/ijcrms.2026.12.01.002	

How to cite this article:
Emmanuel Ifeanyi Obeagu and Amarachi Suzzy-Martins Ezekwunem. (2026). Cytokine Release Syndrome in HIV Infection: Immunopathogenesis, Clinical Features, and Therapeutic and Management Implications. Int. J. Curr. Res. Med. Sci. 12(1): 13-21.
DOI: http://dx.doi.org/10.22192/ijcrms.2026.12.01.002