

Immunological Aspects of HIV Control in Perinatally Infected Infants: A Review

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Abstract

Perinatal HIV infection remains a significant global health challenge, impacting infants born to HIV-positive mothers worldwide. This review synthesizes current knowledge on immune responses in perinatally infected infants, focusing on mechanisms of immune control, viral persistence, and the impact of antiretroviral therapy (ART). Insights into immune development, viral-host interactions, and therapeutic strategies highlight the complexities of HIV pathogenesis in early life and underscore the need for tailored approaches to enhance immune control and mitigate disease progression in this vulnerable population. In perinatally infected infants, immune responses against HIV are characterized by a dynamic interplay between innate and adaptive immunity. Early in infection, natural killer (NK) cells and other innate immune effectors play critical roles in recognizing and responding to HIV-infected cells. However, HIV can evade these initial defenses by establishing viral reservoirs and modulating host immune responses, contributing to persistent viral replication and immune activation. Adaptive immune responses, including T cell-mediated immunity, undergo maturation processes that influence viral control and immune memory formation. Dysregulation of these pathways compromises immune function and increases susceptibility to opportunistic infections in perinatally infected infants. Antiretroviral therapy (ART) represents the cornerstone of HIV management in perinatally infected infants, effectively suppressing viral replication and preserving immune function. Early initiation of ART is essential for preventing disease progression, reducing viral reservoirs, and promoting immune reconstitution.

Keywords: *HIV, perinatal infection, infants, immune responses, immune control, antiretroviral therapy, immune reconstitution*

Introduction

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Perinatal HIV infection continues to pose significant challenges globally, affecting infants born to HIV-positive mothers. Despite advances in prevention of mother-to-child transmission (PMTCT) programs and antiretroviral therapy (ART), perinatal HIV transmission remains a critical issue in regions with high HIV prevalence. Infants acquire HIV either in utero, during childbirth, or through breastfeeding, exposing them to the virus during crucial stages of immune system development. Understanding the immunological aspects of HIV control in perinatally infected infants is paramount for improving treatment strategies and long-term outcomes.¹⁻² The immune responses in perinatally infected infants are characterized by a complex interplay of innate and adaptive immune mechanisms. Shortly after birth, infants are exposed to HIV and mount innate immune responses involving natural killer (NK) cells, macrophages, and dendritic cells. NK cells play a pivotal role in early immune surveillance, recognizing and eliminating HIV-infected cells through cytotoxicity and cytokine production. However, HIV's ability to evade these initial defenses and establish reservoirs contributes to persistent viral replication and chronic immune activation in infected infants. This dynamic interaction between the virus and the developing immune system shapes disease progression and the efficacy of therapeutic interventions.³⁻⁵ The developmental stage of the infant's immune system at the time of HIV exposure significantly influences disease outcomes. Neonatal immune responses are inherently immature, characterized by reduced antigen-presenting capacity, T cell function, and antibody production compared to older children and adults. This immaturity not only impacts the initial immune response to HIV but also affects the establishment of viral reservoirs and the ability to control viral replication. Moreover, the timing and route of HIV transmission (in utero, during delivery, or through breastfeeding) further influence the pattern of immune activation, viral dissemination, and clinical presentation in perinatally infected infants.⁶⁻⁸

Antiretroviral therapy (ART) has revolutionized the management of perinatal HIV infection by effectively suppressing viral replication and preserving immune function. Early initiation of ART is critical for preventing disease progression, reducing viral reservoirs, and restoring immune competence in infected infants. ART regimens typically include combinations of nucleoside reverse transcriptase inhibitors (NRTIs), protease inhibitors (PIs), and integrase strand transfer inhibitors (INSTIs), tailored to inhibit different stages of the HIV lifecycle. However, challenges such as drug adherence, drug resistance, and long-term toxicity necessitate ongoing research to optimize ART regimens for infants, ensuring maximal efficacy and minimal side effects.⁹⁻¹⁰ The impact of ART on immune reconstitution in perinatally infected infants is a critical area of study. Effective suppression of viral replication with ART allows for partial restoration of immune function, including CD4⁺ T cell counts and T cell responsiveness. However, immune reconstitution may be incomplete or delayed in some infants, particularly those with advanced disease or late initiation of therapy. Persistent immune activation and inflammation, despite viral suppression, may contribute to long-term immune dysfunction and increased susceptibility to opportunistic infections. Strategies to enhance immune reconstitution and reduce chronic immune activation are essential for improving long-term health outcomes in perinatally infected infants on ART.¹¹⁻¹²

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Immune correlates of protection against HIV in perinatally infected infants remain incompletely understood but are critical for guiding therapeutic strategies and vaccine development efforts. Studies investigating immune biomarkers, such as cytokine profiles, antibody responses, and cellular immune responses, are essential for identifying predictors of disease progression and treatment outcomes. Moreover, understanding immune mechanisms that contribute to natural control of HIV, observed in a minority of perinatally infected infants known as "elite controllers," offers insights into potential targets for enhancing immune responses and achieving viral remission without ART.¹³⁻¹⁴ The challenges of managing perinatal HIV infection extend beyond medical interventions to encompass social, economic, and ethical considerations. Access to healthcare services, including early HIV testing, timely initiation of ART, and comprehensive pediatric care, remains a significant barrier in resource-limited settings. Social stigma and discrimination associated with HIV can also impact treatment adherence and retention in care for infants and their families. Addressing these multifaceted challenges requires a holistic approach that integrates medical, psychosocial, and public health interventions to optimize outcomes and promote well-being in perinatally infected infants and their caregivers.¹⁵⁻¹⁶ Emerging therapeutic strategies hold promise for improving HIV management in perinatally infected infants. These include immunomodulatory therapies to enhance immune responses, novel antiretroviral agents with improved pharmacokinetics, and gene editing technologies aimed at eliminating viral reservoirs. Advances in understanding host-virus interactions, immune activation pathways, and viral latency reversal are driving innovative approaches towards achieving sustained viral suppression and functional cure in infected infants. Collaborative efforts across disciplines, supported by global healthcare initiatives and community engagement, are essential for translating research discoveries into effective clinical interventions and reducing the global burden of pediatric HIV/AIDS.¹⁷⁻¹⁸

Immune Responses in Perinatally Infected Infants

Immune responses in perinatally infected infants are shaped by a dynamic interaction between the developing immune system and the human immunodeficiency virus (HIV). Upon exposure to HIV, infants initiate innate immune responses as their primary defense mechanism. Natural killer (NK) cells, a key component of innate immunity, play a crucial role in early immune surveillance by recognizing and eliminating HIV-infected cells through cytotoxicity and the release of cytokines such as interferon gamma (IFN- γ) and tumor necrosis factor alpha (TNF- α). However, HIV has evolved strategies to evade NK cell detection, including downregulation of NK cell-activating ligands and modulation of host immune responses, thereby promoting viral persistence.¹⁹⁻²¹ In addition to NK cells, other innate immune cells such as macrophages and dendritic cells contribute to the initial immune response against HIV in perinatally infected infants. These cells recognize viral components through pattern recognition receptors (PRRs) and initiate innate immune signaling pathways, leading to the production of pro-inflammatory cytokines and chemokines that recruit and activate other immune cells. Despite these early immune responses, HIV can establish reservoirs in tissues such as lymph nodes and the central nervous system, where it persists despite antiretroviral therapy (ART). This persistence contributes to chronic immune activation and inflammation, which are hallmarks of HIV infection in infants and can impact long-term immune function.²²⁻²⁴

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Adaptive immune responses in perinatally infected infants are characterized by the development of HIV-specific T cell responses and the production of neutralizing antibodies. CD4⁺ T cells, essential for orchestrating immune responses, are targeted and depleted by HIV, leading to progressive immune dysfunction and increased susceptibility to opportunistic infections. The timing and magnitude of T cell responses are critical determinants of disease progression in infected infants. Infants with more robust T cell responses may exhibit better control of viral replication and slower disease progression, whereas those with impaired T cell function may experience rapid disease progression and poorer outcomes.²⁵⁻²⁶ Furthermore, the maturation of B cells and the production of HIV-specific antibodies play crucial roles in immune defense and vaccine-induced protection. Infants exposed to HIV may generate broadly neutralizing antibodies (bNAbs) against conserved epitopes of the virus, offering potential targets for vaccine development. However, the immature immune system and ongoing viral replication can limit the effectiveness of antibody responses in controlling HIV infection. Strategies to enhance antibody-mediated immunity through passive immunization or vaccine strategies that elicit potent and durable antibody responses are areas of active research in perinatal HIV infection.²⁷⁻²⁸ Despite innate and adaptive immune responses, perinatally infected infants often exhibit persistent immune activation and inflammation, even in the presence of ART-mediated viral suppression. Chronic immune activation is associated with accelerated immune senescence, characterized by premature aging of the immune system and increased susceptibility to non-AIDS-related comorbidities.²⁹⁻³⁰

Viral Persistence and Immune Evasion Strategies

Viral persistence and immune evasion strategies are critical aspects of HIV pathogenesis in perinatally infected infants, influencing disease progression, treatment outcomes, and the quest for a cure. Upon transmission, HIV establishes reservoirs in sanctuary sites such as lymphoid tissues, the central nervous system, and mucosal compartments. These reservoirs allow the virus to evade immune surveillance and persist despite effective antiretroviral therapy (ART). Understanding the mechanisms of viral persistence and immune evasion is essential for developing strategies to achieve viral remission or eradication in infected infants.³¹ One of the key mechanisms contributing to viral persistence is the establishment of latent reservoirs. HIV can integrate its genetic material into the host genome of long-lived cells, such as memory CD4⁺ T cells and macrophages, where it remains transcriptionally silent and evades detection by the immune system. Latently infected cells can persist for years, serving as a source of viral rebound if ART is interrupted. In perinatally infected infants, early seeding of these reservoirs occurs during the neonatal period, potentially influencing the effectiveness of early ART initiation in preventing reservoir establishment and reducing the size of the viral reservoir.³²⁻³³

Moreover, HIV employs multiple immune evasion strategies to evade detection and elimination by the immune system in perinatally infected infants. One of the primary mechanisms involves viral escape from CD8⁺ cytotoxic T lymphocyte (CTL) responses. HIV rapidly mutates due to its error-prone reverse transcriptase enzyme, resulting in the generation of diverse viral quasispecies. These mutations allow the virus to evade recognition by CTLs targeting specific epitopes, thereby reducing the effectiveness of T cell-mediated immune responses and promoting viral persistence.

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Additionally, HIV downregulates major histocompatibility complex class I (MHC-I) molecules on infected cells, impairing antigen presentation and reducing CTL recognition and killing of infected cells.³⁴⁻³⁵ Furthermore, HIV modulates host immune responses to create a microenvironment conducive to viral persistence and immune evasion. The virus induces chronic immune activation characterized by elevated levels of pro-inflammatory cytokines, such as interleukin-6 (IL-6) and tumor necrosis factor alpha (TNF- α), and immune checkpoint pathways, such as PD-1/PD-L1, which dampen immune responses and promote T cell exhaustion. Chronic immune activation contributes to T cell dysfunction, impaired B cell responses, and premature immune senescence in perinatally infected infants, despite ART-mediated viral suppression.³⁶⁻³⁷

Additionally, HIV targets innate immune cells, such as dendritic cells (DCs), macrophages, and natural killer (NK) cells, to evade innate immune responses and establish viral persistence. HIV-infected DCs can facilitate viral dissemination to CD4+ T cells and induce immunosuppressive regulatory T cells (Tregs), which dampen antiviral immune responses. Macrophages serve as reservoirs for productive viral replication and contribute to chronic inflammation in infected tissues. NK cells, critical for early immune surveillance and antiviral defense, are dysfunctional in HIV-infected infants due to downregulation of NK cell-activating receptors and impaired cytotoxicity against infected cells.³⁸⁻³⁹ Moreover, the unique characteristics of the neonatal immune system, including immaturity of adaptive and innate immune responses, contribute to heightened susceptibility to HIV and difficulty in achieving viral control. Neonatal CD4+ T cells are more susceptible to HIV infection and exhibit impaired immune activation and proliferation compared to adult T cells. Immature dendritic cells and monocytes also display reduced antigen-presenting capacity and impaired cytokine production, which limit effective immune responses against HIV. These factors collectively contribute to viral persistence and immune evasion in perinatally infected infants, highlighting the need for targeted therapeutic interventions aimed at restoring immune function and achieving durable viral control.⁴⁰⁻⁴¹

Impact of Antiretroviral Therapy (ART)

Antiretroviral therapy (ART) has revolutionized the management of perinatally acquired HIV infection, significantly altering the landscape of pediatric HIV/AIDS care and improving outcomes for infected infants. The impact of ART extends across multiple dimensions, including viral suppression, immune reconstitution, prevention of opportunistic infections, and overall survival. Early initiation of ART in perinatally infected infants is crucial for maximizing these benefits and mitigating the deleterious effects of HIV on immune function and long-term health.⁴²⁻⁴³ One of the primary objectives of ART in perinatally infected infants is to achieve and maintain viral suppression. ART effectively inhibits HIV replication by targeting key steps in the viral lifecycle, such as reverse transcription, integration, and viral maturation. Suppression of viral replication reduces circulating HIV RNA levels to undetectable or very low levels (<50 copies/mL), preventing viral dissemination and reducing the risk of disease progression. Viral suppression not only improves immediate health outcomes by preserving immune function but also reduces the likelihood of transmitting HIV to uninfected individuals, including caregivers and other children.⁴⁴⁻⁴⁵

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ART-mediated viral suppression is instrumental in preserving immune function and promoting immune reconstitution in perinatally infected infants. Effective suppression of viral replication allows for the recovery of CD4⁺ T cell counts, which are crucial for orchestrating immune responses against pathogens. Restoring CD4⁺ T cell levels improve immune competence, enhances the ability to mount specific immune responses, and reduces susceptibility to opportunistic infections such as *Pneumocystis jirovecii* pneumonia (PCP), cytomegalovirus (CMV) infections, and severe bacterial infections. Immune reconstitution also involves normalization of immune activation markers and reduction of chronic inflammation, which contribute to long-term immune health and quality of life.⁴⁶⁻⁴⁷ In addition to preserving immune function, ART plays a pivotal role in preventing HIV-related morbidity and mortality in perinatally infected infants. Infants who receive early and consistent ART experience fewer HIV-related complications, such as wasting syndrome, HIV encephalopathy, and AIDS-defining illnesses. The reduction in disease burden translates into improved growth and development outcomes, reduced hospitalizations, and prolonged survival. Longitudinal studies have demonstrated that infants who adhere to ART regimens achieve better clinical outcomes, highlighting the importance of adherence support and monitoring in pediatric HIV/AIDS management.⁴⁸⁻⁴⁹

Furthermore, ART contributes to reducing the overall burden of pediatric HIV/AIDS by preventing vertical transmission of HIV from mother to child during pregnancy, childbirth, and breastfeeding. Effective implementation of PMTCT programs, which include maternal ART during pregnancy and breastfeeding, cesarean delivery when indicated, and infant prophylaxis with ART, has led to significant reductions in mother-to-child transmission rates globally. The integration of ART into comprehensive maternal and child health services has been instrumental in achieving the global targets for eliminating new HIV infections among children and ensuring better health outcomes for HIV-exposed infants.⁵⁰⁻⁵¹ However, despite the numerous benefits of ART, challenges remain in its optimal implementation and long-term management in perinatally infected infants. These challenges include ensuring timely diagnosis of HIV infection in infants, selecting appropriate ART regimens based on drug availability, infant age, and comorbidities, addressing issues related to drug adherence and resistance, managing ART-related toxicities, and promoting retention in care throughout childhood and adolescence. Addressing these challenges requires a multidisciplinary approach that includes healthcare providers, policymakers, community stakeholders, and caregivers to optimize ART outcomes and support the well-being of perinatally infected infants and their families.⁵²⁻⁵³

Immune Reconstitution and Long-Term Outcomes

Immune reconstitution in perinatally infected infants undergoing antiretroviral therapy (ART) is a complex process influenced by various factors, including the timing of ART initiation, viral suppression efficacy, immune activation status, and the developmental stage of the infant's immune system. Achieving optimal immune reconstitution is crucial for reducing susceptibility to opportunistic infections, improving overall health outcomes, and potentially achieving long-term viral remission or cure in HIV-infected infants.⁵⁴ Early initiation of ART in perinatally infected infants is associated with more favorable immune reconstitution outcomes. ART suppresses viral

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replication, which helps preserve and restore CD4+ T cell counts, a critical marker of immune function. Restoration of CD4+ T cells enhance the infant's ability to mount specific immune responses against pathogens and vaccines, thereby reducing the risk of opportunistic infections such as *Pneumocystis jirovecii* pneumonia (PCP), cytomegalovirus (CMV) infections, and severe bacterial infections. Studies have shown that infants who initiate ART early in life experience more rapid and complete immune reconstitution compared to those who start treatment later.⁵⁵ However, immune reconstitution in perinatally infected infants may be incomplete or delayed despite effective viral suppression with ART. Persistent immune activation and inflammation, characterized by elevated levels of pro-inflammatory cytokines and immune activation markers, contribute to ongoing immune dysfunction and impaired immune recovery. Chronic immune activation is associated with accelerated immune senescence, premature aging of the immune system, and increased susceptibility to non-AIDS-related comorbidities such as cardiovascular disease and neurocognitive impairment in later life. Strategies to mitigate chronic immune activation and promote immune reconstitution are critical for improving long-term health outcomes in perinatally infected infants.⁵⁶

In addition to CD4+ T cell recovery, immune reconstitution encompasses the restoration of functional immune responses across multiple cell types, including CD8+ T cells, B cells, natural killer (NK) cells, and antigen-presenting cells (APCs). CD8+ T cells play a crucial role in HIV control by recognizing and eliminating HIV-infected cells through cytotoxicity and the release of antiviral cytokines. Effective ART allows for the restoration of CD8+ T cell function, enhancing immune surveillance and contributing to viral suppression. B cell function is essential for the production of HIV-specific antibodies and the generation of humoral immune responses. ART-mediated viral suppression enables the development of robust antibody responses, which may contribute to immune protection and vaccine-induced immunity in infected infants.⁵⁷ Long-term monitoring of immune reconstitution in perinatally infected infants on ART is essential for identifying immune correlates of protection, predicting treatment outcomes, and guiding therapeutic interventions. Immune biomarkers, such as CD4+ T cell counts, CD4/CD8 ratio, cytokine profiles, and T cell receptor diversity, provide insights into immune status and may serve as predictors of disease progression and therapeutic response. Comprehensive immune monitoring strategies should be integrated into routine clinical care to optimize ART management, identify early signs of immune dysfunction, and tailor therapeutic interventions to individual patient needs.⁵⁸

Emerging Therapeutic Strategies and Future Directions

Emerging therapeutic strategies for perinatally infected infants with HIV aim to address challenges such as viral persistence, immune dysfunction, and long-term complications, despite the successes of antiretroviral therapy (ART). These strategies encompass innovative approaches that target viral reservoirs, enhance immune responses, and ultimately aim for functional cure or sustained viral remission. One promising area of research focuses on targeting and eliminating HIV reservoirs, particularly latent viral reservoirs that persist despite ART. Strategies under investigation include latency-reversing agents (LRAs) that aim to activate latent HIV, making it susceptible to immune

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clearance or eradication strategies. LRAs such as histone deacetylase inhibitors (HDAC inhibitors), toll-like receptor agonists, and immune checkpoint inhibitors are being evaluated in clinical trials to assess their ability to induce viral transcription and reduce the size of latent reservoirs. Combinations of LRAs with immune modulators and therapeutic vaccines are being explored to maximize the effectiveness of reservoir clearance strategies.⁵⁹ Gene editing technologies, such as CRISPR-Cas9, offer promising avenues for targeting and disrupting HIV proviral DNA integrated into host genomes. CRISPR-based approaches aim to achieve precise editing of viral DNA sequences within infected cells, potentially leading to permanent inactivation or elimination of viral reservoirs. Challenges such as delivery methods, off-target effects, and ethical considerations are being addressed through ongoing research to optimize the safety and efficacy of gene editing strategies in clinical settings.

Immunomodulatory therapies represent another frontier in pediatric HIV/AIDS research, focusing on enhancing immune responses to achieve durable viral control and immune reconstitution. Strategies include therapeutic vaccines designed to elicit potent and broad HIV-specific immune responses, including cytotoxic T lymphocyte (CTL) responses and neutralizing antibodies. Vaccine candidates targeting conserved regions of the HIV envelope glycoprotein, such as mosaic vaccines and HIV DNA vaccines, are being evaluated in clinical trials to assess their safety, immunogenicity, and potential efficacy in reducing viral reservoirs and preventing viral rebound after ART interruption.⁵⁶ Furthermore, immune-based therapies such as immune checkpoint inhibitors (ICIs) are being explored to enhance immune responses against HIV. ICIs block inhibitory signals that dampen immune responses, thereby potentially restoring T cell function and enhancing immune surveillance against HIV-infected cells. Combination therapies incorporating ICIs with LRAs or therapeutic vaccines aim to synergistically enhance immune activation and improve control over viral replication, offering new avenues for achieving long-term immune control and functional cure in perinatally infected infants.⁵⁸ In addition to novel therapeutic approaches, advancements in ART regimens continue to improve treatment outcomes and quality of life for perinatally infected infants. Long-acting formulations of antiretroviral drugs, such as injectable formulations and implantable devices, offer potential benefits in improving treatment adherence and reducing the frequency of drug administration. Simplified ART regimens with fewer side effects and improved pharmacokinetic profiles are being developed to optimize therapeutic outcomes and minimize treatment-related toxicity in pediatric populations.⁵⁹

Conclusion

The management of perinatally acquired HIV infection has evolved significantly with the advent of antiretroviral therapy (ART), yet challenges persist in achieving long-term viral suppression and immune reconstitution in infected infants. ART remains the cornerstone of treatment, effectively suppressing viral replication, preserving immune function, and improving overall health outcomes. Early initiation of ART, ideally soon after birth or diagnosis, is crucial for maximizing these benefits and reducing the establishment of viral reservoirs that contribute to persistent infection. Despite the successes of ART, achieving sustained viral remission or functional cure remains elusive. Viral persistence in reservoirs and chronic immune activation

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continue to pose significant barriers to achieving durable control over HIV replication. Emerging therapeutic strategies such as latency-reversing agents, gene editing technologies, and immunomodulatory therapies hold promise for targeting latent viral reservoirs, enhancing immune responses, and potentially achieving long-term viral remission without continuous ART. Immune reconstitution in perinatally infected infants is a complex process influenced by the timing of ART initiation, viral suppression efficacy, and the developmental stage of the infant's immune system. Strategies to mitigate chronic immune activation, restore immune function, and prevent immune exhaustion are essential for improving long-term health outcomes and reducing the risk of non-AIDS-related comorbidities. Comprehensive immune monitoring and personalized treatment approaches are critical for optimizing ART management and tailoring therapeutic interventions to individual patient needs.

References

1. Yu JC, Khodadadi H, Malik A, Davidson B, Salles ÉD, Bhatia J, Hale VL, Baban B. Innate immunity of neonates and infants. *Frontiers in immunology*. 2018; 9:1759.
2. Goenka A, Kollmann TR. Development of immunity in early life. *Journal of Infection*. 2015;71: S112-120.
3. Lewis DB, Weitkamp JH, Levy O. Developmental immunology and role of host defenses in fetal and neonatal susceptibility to infection. In *Remington and Klein's Infectious Diseases of the Fetus and Newborn Infant 2025*: 73-159. Elsevier.
4. Obeagu EI, Anyiam AF, Obeagu GU. Managing Anemia in HIV through Blood Transfusions: Clinical Considerations and Innovations. *Elite Journal of HIV*, 2024; 2(1): 16-30
5. Obeagu EI, Obeagu, GU. Counting Cells, Shaping Fates: CD4/CD8 Ratios in HIV. *Elite Journal of Scientific Research and Review*, 2024; 2(1): 37-50
6. Obeagu EI, Obeagu GU. Eosinophil Dynamics in Pregnancy among Women Living with HIV: A Comprehensive Review. *Int. J. Curr. Res. Med. Sci.* 2024;10(1):11-24.
7. Obeagu EI, Obeagu GU, Hauwa BA, Umar AI. Neutrophil Dynamics: Unveiling Their Role in HIV Progression within Malaria Patients. *Journal home page*: <http://www.journalijiar.com>;12(01).
8. Obeagu EI, Obeagu, GU. P-Selectin and Platelet Activation in HIV: Implications for Antiviral Therapy. *Elite Journal of Scientific Research and Review*, 2024; 2(1): 17-41
9. Obeagu EI, Obeagu GU. The Intricate Relationship Between Erythropoietin and HIV-Induced Anemia: Unraveling Pathways for Therapeutic Insights. *Int. J. Curr. Res. Chem. Pharm. Sci.* 2024;11(2):30-40.
10. Obeagu EI, Anyiam AF, Obeagu GU. Erythropoietin Therapy in HIV-Infected Individuals: A Critical Review. *Elite Journal of HIV*, 2024; 2(1): 51-64
11. Obeagu EI, Obeagu GU. Strength in Unity: Building Support Networks for HIV Patients in Uganda. *Elite Journal of Medicine*, 2024; 2(1): 1-16
12. Obeagu EI, Obeagu GU. Eosinophilic Changes in Placental Tissues of HIV-Positive Pregnant Women: A Review. *Elite Journal of Laboratory Medicine*, 2024; 2(1): 14-32

Citation: Obeagu EI, Obeagu GU. Immunological Aspects of HIV Control in Perinatally Infected Infants: A Review. *Elite Journal of Immunology*, 2024; 2(6): 1-14

13. Kuhn L, Meddows-Taylor S, Gray G, Tiemessen C. Human immunodeficiency virus (HIV)–specific cellular immune responses in newborns exposed to HIV in utero. *Clinical infectious diseases*. 2002;34(2):267-276.
14. Muenchhoff M, Prendergast AJ, Goulder PJ. Immunity to HIV in early life. *Frontiers in immunology*. 2014; 5:391.
15. Geng ST, Zhang ZY, Wang YX, Lu D, Yu J, Zhang JB, Kuang YQ, Wang KH. Regulation of gut microbiota on immune reconstitution in patients with acquired immunodeficiency syndrome. *Frontiers in microbiology*. 2020; 11:594820.
16. Obeagu EI, Obeagu GU. The Crucial Role of Erythropoietin in Managing Anemia in HIV: A Review. *Elite Journal of Scientific Research and Review*, 2024; 2(1): 24-36
17. Obeagu EI, Ubosi NI, Obeagu GU, Obeagu AA. Nutritional Strategies for Enhancing Immune Resilience in HIV: A Review. *Int. J. Curr. Res. Chem. Pharm. Sci*. 2024;11(2):41-51.
18. Obeagu EI, Obeagu GU. Assessing Platelet Functionality in HIV Patients Receiving Antiretroviral Therapy: Implications for Risk Assessment. *Elite Journal of HIV*, 2024; 2(3): 14-26
19. Obeagu EI, Elamin EAI Obeagu GU. Understanding the Intersection of Highly Active Antiretroviral Therapy and Platelets in HIV Patients: A Review. *Elite Journal of Haematology*, 2024; 2(3): 111-117
20. Obeagu EI, Obeagu GU. Understanding ART and Platelet Functionality: Implications for HIV Patients. *Elite Journal of HIV*, 2024; 2(2): 60-73
21. Obeagu EI, Obeagu GU. Neonatal Outcomes in Children Born to Mothers with Severe Malaria, HIV, and Transfusion History: A Review. *Elite Journal of Nursing and Health Science*, 2024; 2(3): 38-58
22. Obeagu EI. Erythropoietin and the Immune System: Relevance in HIV Management. *Elite Journal of Health Science*, 2024; 2(3): 23-35
23. Obeagu EI, Obeagu GU. Understanding Immune Cell Trafficking in Tuberculosis-HIV Coinfection: The Role of L-selectin Pathways. *Elite Journal of Immunology*, 2024; 2(2): 43-59
24. Obeagu EI, Obeagu GU. Anemia and Erythropoietin: Key Players in HIV Disease Progression. *Elite Journal of Haematology*, 2024; 2(3): 42-57
25. Obeagu EI, Ayogu EE, Obeagu GU. Impact on Viral Load Dynamics: Understanding the Interplay between Blood Transfusion and Antiretroviral Therapy in HIV Management. *Elite Journal of Nursing and Health Science*, 2024; 2(2): 5-15
26. Obeagu EI, Obeagu GU. Immune Modulation in HIV-Positive Neonates: Insights and Implications for Clinical Management. *Elite Journal of Nursing and Health Science*, 2024; 2(3): 59-72
27. Ifeanyi OE, Obeagu GU. The values of prothrombin time among HIV positive patients in FMC owerri. *International Journal of Current Microbiology and Applied Sciences*. 2015;4(4):911-916.
https://www.academia.edu/download/38320140/Obeagu_Emanuel_Ifeanyi_and_Obeagu_Getrude_Uzoma2.EMMA1.pdf.

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28. Yu JC, Khodadadi H, Malik A, Davidson B, Salles ÉD, Bhatia J, Hale VL, Baban B. Innate immunity of neonates and infants. *Frontiers in immunology*. 2018; 9:1759.
29. Levy O. Innate immunity of the newborn: basic mechanisms and clinical correlates. *Nature Reviews Immunology*. 2007;7(5):379-390.
30. Pieren DK, Boer MC, de Wit J. The adaptive immune system in early life: The shift makes it count. *Frontiers in immunology*. 2022; 13:1031924.
31. Rackaityte E, Halkias J. Mechanisms of fetal T cell tolerance and immune regulation. *Frontiers in immunology*. 2020; 11:588.
32. Sereme Y, Toumi E, Saifi E, Faury H, Skurnik D. Maternal immune factors involved in the prevention or facilitation of neonatal bacterial infections. *Cellular Immunology*. 2024; 395:104796.
33. Zhang X, Zhivaki D, Lo-Man R. Unique aspects of the perinatal immune system. *Nature Reviews Immunology*. 2017;17(8):495-507.
34. Sanidad KZ, Zeng MY. Neonatal gut microbiome and immunity. *Current opinion in microbiology*. 2020; 56:30-37.
35. Izuchukwu IF, Ozims SJ, Agu GC, Obeagu EI, Onu I, Amah H, Nwosu DC, Nwanjo HU, Edward A, Arunsi MO. Knowledge of preventive measures and management of HIV/AIDS victims among parents in Umuna Orlu community of Imo state Nigeria. *Int. J. Adv. Res. Biol. Sci.* 2016;3(10): 55-65.DOI; [10.22192/ijarbs.2016.03.10.009](https://doi.org/10.22192/ijarbs.2016.03.10.009)
36. Chinedu K, Takim AE, Obeagu EI, Chinazor UD, Eloghosa O, Ojong OE, Odunze U. HIV and TB co-infection among patients who used Directly Observed Treatment Short-course centres in Yenagoa, Nigeria. *IOSR J Pharm Biol Sci.* 2017;12(4):70-75. [links/5988ab6d0f7e9b6c8539f73d/HIV-and-TB-co-infection-among-patients-who-used-Directly-Observed-Treatment-Short-course-centres-in-Yenagoa-Nigeria.pdf](https://www.iosrjournals.org/IOSRjournal/index.php/IOSRJP/article/view/5988ab6d0f7e9b6c8539f73d/HIV-and-TB-co-infection-among-patients-who-used-Directly-Observed-Treatment-Short-course-centres-in-Yenagoa-Nigeria.pdf)
37. Oloro OH, Oke TO, Obeagu EI. Evaluation of Coagulation Profile Patients with Pulmonary Tuberculosis and Human Immunodeficiency Virus in Owo, Ondo State, Nigeria. *Madonna University journal of Medicine and Health Sciences*. 2022;2(3):110-119.
38. Nwosu DC, Obeagu EI, Nkwocha BC, Nwanna CA, Nwanjo HU, Amadike JN, Elendu HN, Ofoedeme CN, Ozims SJ, Nwankpa P. Change in Lipid Peroxidation Marker (MDA) and Non enzymatic Antioxidants (VIT C & E) in HIV Seropositive Children in an Urban Community of Abia State. Nigeria. *J. Bio. Innov.* 2016;5(1):24-30. [links/5ae735e9a6fdcc5b33eb8d6a/CHANGE-IN-LIPID-PEROXIDATION-MARKER-MDAAND-NON-ENZYMATIC-ANTIOXIDANTS-VIT-C-E-IN-HIV-SEROPOSITIVE-CHILDREN-IN-AN-URBAN-COMMUNITY-OF-ABIA-STATE-NIGERIA.pdf](https://www.iosrjournals.org/IOSRjournal/index.php/IOSRJP/article/view/5ae735e9a6fdcc5b33eb8d6a/CHANGE-IN-LIPID-PEROXIDATION-MARKER-MDAAND-NON-ENZYMATIC-ANTIOXIDANTS-VIT-C-E-IN-HIV-SEROPOSITIVE-CHILDREN-IN-AN-URBAN-COMMUNITY-OF-ABIA-STATE-NIGERIA.pdf).
39. Ifeanyi OE, Obeagu GU, Ijeoma FO, Chioma UI. The values of activated partial thromboplastin time (APTT) among HIV positive patients in FMC Owerri. *Int J Curr Res Aca Rev.* 2015; 3:139-144. https://www.academia.edu/download/38320159/Obeagu_Emanuel_Ifeanyi3_et_al.IJC_RAR.pdf.
40. Obiomah CF, Obeagu EI, Ochei KC, Swem CA, Amachukwu BO. Hematological indices o HIV seropositive subjects in Nnamdi Azikiwe University teaching hospital (NAUTH), Nnewi. *Ann Clin Lab Res.* 2018;6(1):1-4.

Citation: Obeagu EI, Obeagu GU. Immunological Aspects of HIV Control in Perinatally Infected Infants: A Review. *Elite Journal of Immunology*, 2024; 2(6): 1-14

[links/5aa2bb17a6fdccd544b7526e/Haematological-Indices-of-HIV-Seropositive-Subjects-at-Nnamdi-Azikiwe.pdf](https://www.academia.edu/download/54317126/Haematological_indices_of_malaria_patients_coinfected_with_HIV.pdf)

41. Omo-Emmanuel UK, Ochei KC, Osuala EO, Obeagu EI, Onwuasoanya UF. Impact of prevention of mother to child transmission (PMTCT) of HIV on positivity rate in Kafanchan, Nigeria. *Int. J. Curr. Res. Med. Sci.* 2017;3(2): 28-34.DOI: [10.22192/ijcrms.2017.03.02.005](https://doi.org/10.22192/ijcrms.2017.03.02.005)
42. Aizaz M, Abbas FA, Abbas A, Tabassum S, Obeagu EI. Alarming rise in HIV cases in Pakistan: Challenges and future recommendations at hand. *Health Science Reports.* 2023;6(8):e1450.
43. Obeagu EI, Amekpor F, Scott GY. An update of human immunodeficiency virus infection: Bleeding disorders. *J Pub Health Nutri.* 2023; 6 (1). 2023;139. [links/645b4a6c2edb8e5f094d9bd9/An-update-of-human-immunodeficiency-virus-infection-Bleeding.pdf](https://www.academia.edu/download/54317126/An-update-of-human-immunodeficiency-virus-infection-Bleeding.pdf).
44. Obeagu EI, Scott GY, Amekpor F, Ofodile AC, Edoho SH, Ahamefula C. Prevention of New Cases of Human Immunodeficiency Virus: Pragmatic Approaches of Saving Life in Developing Countries. *Madonna University journal of Medicine and Health Sciences.* 2022;2(3):128-134. <https://madonnauniversity.edu.ng/journals/index.php/medicine/article/view/86>.
45. Walter O, Anaabo QB, Obeagu EI, Okoroiwu IL. Evaluation of Activated Partial Thromboplastin Time and Prothrombin Time in HIV and TB Patients in Owerri Metropolis. *Journal of Pharmaceutical Research International.* 2022:29-34.
46. Odo M, Ochei KC, Obeagu EI, Barinaadaa A, Eteng EU, Ikpeme M, Bassey JO, Paul AO. Cascade variabilities in TB case finding among people living with HIV and the use of IPT: assessment in three levels of care in cross River State, Nigeria. *Journal of Pharmaceutical Research International.* 2020;32(24):9-18.
47. Obeagu EI, Obeagu GU. A Review of knowledge, attitudes and socio-demographic factors associated with non-adherence to antiretroviral therapy among people living with HIV/AIDS. *Int. J. Adv. Res. Biol. Sci.* 2023;10(9):135-142.DOI: [10.22192/ijarbs.2023.10.09.015](https://doi.org/10.22192/ijarbs.2023.10.09.015) [links/6516faa61e2386049de5e828/A-Review-of-knowledge-attitudes-and-socio-demographic-factors-associated-with-non-adherence-to-antiretroviral-therapy-among-people-living-with-HIV-AIDS.pdf](https://www.academia.edu/download/54317126/A-Review-of-knowledge-attitudes-and-socio-demographic-factors-associated-with-non-adherence-to-antiretroviral-therapy-among-people-living-with-HIV-AIDS.pdf)
48. Obeagu EI, Onuoha EC. Tuberculosis among HIV Patients: A review of Prevalence and Associated Factors. *Int. J. Adv. Res. Biol. Sci.* 2023;10(9):128-134.DOI: [10.22192/ijarbs.2023.10.09.014](https://doi.org/10.22192/ijarbs.2023.10.09.014) [links/6516f938b0df2f20a2f8b0e0/Tuberculosis-among-HIV-Patients-A-review-of-Prevalence-and-Associated-Factors.pdf](https://www.academia.edu/download/54317126/Tuberculosis-among-HIV-Patients-A-review-of-Prevalence-and-Associated-Factors.pdf).
49. Obeagu EI, Ibeh NC, Nwobodo HA, Ochei KC, Iwegbulam CP. Haematological indices of malaria patients coinfecting with HIV in Umuahia. *Int. J. Curr. Res. Med. Sci.* 2017;3(5):100-104.DOI: [10.22192/ijcrms.2017.03.05.014](https://doi.org/10.22192/ijcrms.2017.03.05.014) [https://www.academia.edu/download/54317126/Haematological indices of malaria patients coinfecting with HIV.pdf](https://www.academia.edu/download/54317126/Haematological_indices_of_malaria_patients_coinfected_with_HIV.pdf)
50. Okorie HM, Obeagu Emmanuel I, Okpoli Henry CH, Chukwu Stella N. Comparative study of enzyme linked immunosorbent assay (Elisa) and rapid test screening methods on HIV, Hbsag, Hcv and Syphilis among voluntary donors in. Owerri, Nigeria. *J Clin Commun*

Citation: Obeagu EI, Obeagu GU. Immunological Aspects of HIV Control in Perinatally Infected Infants: A Review. *Elite Journal of Immunology*, 2024; 2(6): 1-14

- Med. 2020;2(3):180-183.DOI: **DOI:** [10.32474/JCCM.2020.02.000137links/5f344530458515b7291bd95f/Comparative-Study-of-Enzyme-Linked-Immunosorbent-Assay-ELISA-and-Rapid-Test-Screening-Methods-on-HIV-HBsAg-HCV-and-Syphilis-among-Voluntary-Donors-in-Owerri-Nigeria.pdf](https://doi.org/10.32474/JCCM.2020.02.000137links/5f344530458515b7291bd95f/Comparative-Study-of-Enzyme-Linked-Immunosorbent-Assay-ELISA-and-Rapid-Test-Screening-Methods-on-HIV-HBsAg-HCV-and-Syphilis-among-Voluntary-Donors-in-Owerri-Nigeria.pdf).
51. Emmanuel G, Martin O, Peter OS, Obeagu EI, Daniel K. Factors Influencing Early Neonatal Adverse Outcomes among Women with HIV with Post Dated Pregnancies Delivering at Kampala International University Teaching Hospital, Uganda. Asian Journal of Pregnancy and Childbirth. 2023 Jul 29;6(1):203-211. <http://research.sdpublishers.net/id/eprint/2819/>.
 52. Vincent CC, Obeagu EI, Agu IS, Ukeagu NC, Onyekachi-Chigbu AC. Adherence to Antiretroviral Therapy among HIV/AIDS in Federal Medical Centre, Owerri. Journal of Pharmaceutical Research International. 2021;33(57A):360-368.
 53. Madekwe CC, Madekwe CC, Obeagu EI. Inequality of monitoring in Human Immunodeficiency Virus, Tuberculosis and Malaria: A Review. Madonna University journal of Medicine and Health Sciences. 2022;2(3):6-15. <https://madonnauniversity.edu.ng/journals/index.php/medicine/article/view/69>
 54. Echendu GE, Vincent CC, Ibebuikwe J, Asodike M, Naze N, Chinedu EP, Ohale B, Obeagu EI. WEIGHTS OF INFANTS BORN TO HIV INFECTED MOTHERS: A PROSPECTIVE COHORT STUDY IN FEDERAL MEDICAL CENTRE, OWERRI, IMO STATE. European Journal of Pharmaceutical and Medical Research, 2023; 10(8): 564-568
 55. Wilson EM, Sereti I. Immune restoration after antiretroviral therapy: the pitfalls of hasty or incomplete repairs. Immunological reviews. 2013;254(1):343-354.
 56. Misgena DK. The pattern of immunologic and virologic responses to Highly Active Antiretroviral Treatment (HAART): Does success bring further challenges? Ethiopian Journal of Health Development. 2011;25(1):61-70.
 57. Davenport MP, Khoury DS, Cromer D, Lewin SR, Kelleher AD, Kent SJ. Functional cure of HIV: the scale of the challenge. Nature Reviews Immunology. 2019;19(1):45-54.
 58. Geretti AM, Brook G, Cameron C, Chadwick D, French N, Heyderman R, Ho A, Hunter M, Ladhani S, Lawton M, MacMahon E. British HIV Association guidelines on the use of vaccines in HIV-positive adults 2015. HIV medicine. 2016;17(53):S2-81.
 59. Laupèze B, Del Giudice G, Doherty MT, Van der Most R. Vaccination as a preventative measure contributing to immune fitness. npj Vaccines. 2021;6(1):93.

Citation: Obeagu EI, Obeagu GU. Immunological Aspects of HIV Control in Perinatally Infected Infants: A Review. Elite Journal of Immunology, 2024; 2(6): 1-14