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HIV and Innate Immune Memory in Neonates

*Emmanuel Ifeanyi Obeagu

Department of Medical Laboratory Science, Kampala International University, Uganda.

*Corresponding authour: Emmanuel Ifeanyi Obeagu, Department of Medical Laboratory Science, Kampala International University, Uganda, emmanuelobeagu@yahoo.com, ORCID: 0000-0002-4538-0161

Abstract

The interplay between HIV and the neonatal immune system presents significant challenges, particularly in understanding the mechanisms of innate immune memory. Innate immune memory, also known as trained immunity, involves the enhanced response of innate immune cells upon re-exposure to pathogens, a concept traditionally associated with adaptive immunity. This review explores how HIV affects innate immune memory in neonates, emphasizing the unique vulnerabilities and adaptive responses in this population. By delving into the modulation of innate immune cells by HIV, the impact of antiretroviral therapy (ART), and the influence of co-infections and vaccinations, we aim to provide a comprehensive understanding of these complex interactions. Neonates born to HIV-positive mothers, whether infected or HIV-exposed uninfected (HEU), exhibit distinct immune profiles that affect their health outcomes. HIV-infected neonates often show impaired innate immune responses and increased susceptibility to infections, while HEU infants display altered cytokine production and immune cell functions. These differences underscore the need for targeted therapeutic strategies that address the unique immune challenges faced by neonates in the context of HIV exposure and infection. Advancements in understanding innate immune memory in HIV-exposed neonates can inform the development of novel therapeutic interventions. Enhancing innate immune responses, optimizing ART regimens, and developing effective vaccination strategies are potential approaches to improve health outcomes for these vulnerable infants.

Keywords: HIV, innate immune memory, neonates, vertical transmission, immune system development

Introduction

The human immunodeficiency virus (HIV) continues to pose a significant global health challenge, with approximately 38 million people living with the virus as of 2021. Among the most vulnerable populations are neonates born to HIV-positive mothers, who face unique risks and challenges due to their developing immune systems. Vertical transmission of HIV, which can occur during pregnancy, labor, delivery, or breastfeeding, remains a critical concern despite advances in antiretroviral therapy (ART). The implementation of ART has significantly reduced mother-to-child transmission rates; however, the complexities of neonatal immune responses to HIV exposure and infection necessitate further investigation.[1-4] Neonates possess an immune system that is distinct from adults, characterized by a high degree of plasticity and ongoing development.[5] The innate immune system, the first line of defense against pathogens, plays a crucial role in the immediate response to infections in neonates. Key components of the neonatal innate immune

system include pattern recognition receptors (PRRs), natural killer (NK) cells, monocytes, macrophages, and a variety of cytokines and chemokines. These elements work in concert to detect and respond to pathogens, setting the stage for adaptive immune responses. Innate immune memory, or trained immunity, is a relatively new concept that challenges the traditional dichotomy between innate and adaptive immunity.[6] Trained immunity refers to the enhanced responsiveness of innate immune cells, such as monocytes, macrophages, and NK cells, upon re-exposure to pathogens. This phenomenon is mediated by epigenetic reprogramming and metabolic changes that enable a more robust and rapid response to subsequent infections.

HIV infection can modulate the function and phenotype of innate immune cells, potentially impairing their ability to develop trained immunity. The virus employs various mechanisms to evade immune detection and subvert host defenses, including the alteration of PRR signaling pathways and the induction of chronic immune activation. These changes can have profound effects on the ability of neonatal innate immune cells to respond to infections and may compromise the development of effective immune memory.[7-9] The impact of antiretroviral therapy (ART) on innate immune responses in neonates is a critical area of research. ART not only reduces viral load but also affects the function of immune cells. For instance, ART can restore some aspects of immune function in HIV-infected individuals, but its effects on the developing immune system of neonates are not fully understood. Studying how ART influences innate immune memory in neonates exposed to HIV can provide insights into optimizing treatment regimens to support immune health.[10-12] Neonates born to HIV-positive mothers can be classified into two main groups: HIV-infected and HIV-exposed uninfected (HEU).[13-14] HIV-infected neonates face significant challenges due to impaired innate immune responses and increased susceptibility to opportunistic infections. These infants often exhibit altered immune cell functions, including diminished cytokine production and reduced NK cell activity, which can hinder their ability to control infections and respond to vaccinations effectively. HIV-exposed uninfected (HEU) infants also present unique immunological profiles. Although they do not acquire the virus, HEU infants display altered immune responses compared to unexposed infants. These alterations may include changes in cytokine production, immune cell distribution, and increased susceptibility to infections.[15-19] Co-infections and vaccinations play significant roles in shaping the immune responses of HIV-exposed neonates. Co-infections with other pathogens, such as cytomegalovirus (CMV), can further complicate the immune landscape, potentially influencing the development of trained immunity. Vaccination strategies aimed at inducing trained immunity in neonates could offer a promising avenue for enhancing their ability to combat infections and improve overall immune health. The development of therapeutic interventions that leverage the principles of trained immunity holds promise for improving the health outcomes of HIV-exposed neonates. Enhancing innate immune responses through the use of immune modulators, cytokines, or other agents could help boost the ability of neonates to fight infections. Additionally, optimizing ART regimens to not only suppress viral replication but also support immune function in neonates is a critical goal.[20-25]

Innate Immune System in Neonates

The innate immune system is the body's first line of defense against pathogens and plays a critical role in the immediate response to infections.[26] In neonates, the innate immune system is

particularly important as their adaptive immune system is still developing. The neonatal innate immune system is characterized by its unique components and responses, which differ from those in adults, reflecting the need to protect the infant during a period of rapid growth and development. **Pattern Recognition Receptors (PRRs)** are crucial for detecting pathogen-associated molecular patterns (PAMPs) and damage-associated molecular patterns (DAMPs), initiating immune responses.[27] Toll-like receptors (TLRs) are a primary class of PRRs that recognize a wide array of microbial components. In neonates, TLR expression and signaling can be different from adults, often showing a reduced inflammatory response to avoid excessive tissue damage during development. This modulation helps balance the need for effective pathogen defense with the prevention of inflammatory injury. **Natural Killer (NK) Cells** cells are critical for controlling viral infections by recognizing and killing infected cells.[28] Neonatal NK cells are present and functional, but their activity can be lower compared to adults. This reduced activity is partly due to the higher expression of inhibitory receptors and the lower expression of activating receptors. However, neonatal NK cells can still respond robustly to certain stimuli, and their function can be enhanced by cytokines, making them important players in early immune responses.

Monocytes and macrophages are essential for phagocytosis and the production of pro-inflammatory cytokines.[29] In neonates, these cells are adapted to support tissue growth and repair while also providing antimicrobial defense. Neonatal monocytes often produce lower levels of pro-inflammatory cytokines in response to TLR stimulation, which may help protect against excessive inflammation. Macrophages in neonates are also involved in promoting tissue homeostasis and resolving inflammation, reflecting their dual role in defense and development. Cytokines and chemokines are signaling molecules that regulate immune responses and facilitate communication between immune cells. Neonates produce a distinct cytokine profile, often skewed towards anti-inflammatory responses to minimize tissue damage.[30] Key cytokines, such as interleukin-10 (IL-10) and transforming growth factor-beta (TGF-β), play significant roles in modulating neonatal immune responses. The balance between pro-inflammatory and anti-inflammatory cytokines is crucial for effective pathogen defense while preventing harmful inflammation. The complement system is an important part of the innate immune system, consisting of proteins that enhance the ability of antibodies and phagocytic cells to clear pathogens. Neonatal complement activity is generally lower than in adults, which can influence the efficiency of pathogen clearance and immune complex formation.[31] However, the complement system in neonates is still functional and can be rapidly activated in response to infections. Physical and chemical barriers, such as the skin and mucosal surfaces, are crucial components of the innate immune system. In neonates, these barriers are still developing and can be more permeable to pathogens. The skin of neonates, for example, has a thinner stratum corneum and different lipid composition compared to adults, which can influence its barrier function. Additionally, the production of antimicrobial peptides, which are part of the chemical barrier, can be different in neonates. The neonatal innate immune system is adapted to the unique environment of early life, which includes exposure to maternal antibodies, breastfeeding, and the microbiome. Maternal antibodies, transferred through the placenta and breast milk, provide critical passive immunity that helps protect neonates from infections. Breastfeeding also supports the development of the

neonatal immune system by providing immunomodulatory factors and promoting a healthy microbiome, which is essential for immune development.

HIV and Innate Immune Memory

Innate immune memory, also known as trained immunity, is a recently recognized phenomenon wherein innate immune cells, such as monocytes, macrophages, and natural killer (NK) cells, exhibit an enhanced response to subsequent infections following initial exposure to a pathogen or microbial product. This concept challenges the traditional view that only adaptive immunity, characterized by T and B cell responses, possesses memory capabilities. The mechanisms underlying trained immunity involve epigenetic reprogramming and metabolic changes that allow innate immune cells to respond more robustly to future challenges. HIV infection can significantly alter the function and phenotype of innate immune cells, potentially impairing their ability to develop trained immunity. HIV has evolved multiple strategies to evade the host immune system, including the direct infection of key immune cells and the induction of chronic immune activation. For instance, HIV can infect monocytes and macrophages, leading to altered cytokine production and impaired phagocytic function. These changes can hinder the ability of these cells to develop and maintain trained immunity, reducing their effectiveness in responding to subsequent infections.[32-36] NK cells play a crucial role in controlling viral infections by recognizing and killing infected cells. In the context of HIV, NK cell function is often compromised. HIV can downregulate the expression of activating receptors on NK cells and upregulate inhibitory receptors, reducing their cytotoxic activity. Additionally, chronic HIV infection is associated with the exhaustion of NK cells, characterized by reduced proliferative capacity and cytokine production. These alterations can impair the ability of NK cells to develop and retain trained immunity, affecting their ability to respond to other infections.[37-38]

The introduction of ART has revolutionized the management of HIV infection, significantly reduced viral load and improved immune function in infected individuals.[39] However, the effects of ART on the innate immune system, particularly in neonates, are complex and not fully understood. ART can help restore some aspects of innate immune function by reducing viral replication and chronic immune activation. However, ART regimens themselves may also have direct effects on innate immune cells, influencing their ability to develop trained immunity. Investigating how different ART regimens impact trained immunity in neonates exposed to HIV is essential for optimizing treatment strategies. Neonates exposed to HIV are often at increased risk for co-infections with other pathogens, such as cytomegalovirus (CMV) and tuberculosis (TB).[40] These co-infections can further complicate the immune landscape and influence the development of trained immunity. For example, co-infection with CMV has been shown to modulate NK cell function and may impact their ability to develop trained immunity. Additionally, vaccination strategies aimed at inducing trained immunity in neonates could offer a promising avenue for enhancing their ability to combat infections. Vaccines that effectively stimulate trained immunity could provide long-lasting protection and improve overall immune health in HIV-exposed neonates.

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The mechanisms of trained immunity involve epigenetic modifications and metabolic reprogramming of innate immune cells. Epigenetic changes, such as histone modifications and DNA methylation, can alter gene expression patterns, leading to enhanced responsiveness of innate immune cells to subsequent challenges. Metabolic reprogramming, including shifts in glycolysis and mitochondrial function, also plays a critical role in sustaining trained immunity. HIV infection and ART can influence these epigenetic and metabolic pathways, potentially affecting the ability of innate immune cells to develop and maintain trained immunity.[41] Therapeutic interventions that enhance innate immune responses could improve the ability of neonates to combat HIV and other infections.[42] Potential strategies include the use of immune modulators, cytokine therapy, and metabolic reprogramming agents to boost the function and training of innate immune cells. Additionally, optimizing ART regimens to support the development of trained immunity in neonates is crucial for improving long-term health outcomes.

Neonatal Immune Response to HIV

The neonatal immune response to HIV is a critical area of study, given the unique immunological challenges faced by infants born to HIV-positive mothers.[43-44] HIV-infected and HIV-exposed uninfected (HEU). Each group exhibits distinct immune responses, with significant implications for their immediate and long-term health outcomes. Neonates who acquire HIV infection from their mothers face considerable immunological challenges.[45] HIV primarily targets CD4+ T cells, leading to their depletion and compromised immune function. In neonates, this results in an impaired ability to mount effective immune responses to various pathogens. Key aspects of the neonatal immune response to HIV include: HIV-infected neonates often exhibit dysregulated innate immune responses. Monocytes and macrophages, crucial for early pathogen defense, show altered cytokine production and reduced phagocytic activity. These changes hinder the ability to control infections effectively and contribute to a heightened risk of opportunistic infections. NK cells play a vital role in controlling viral infections by recognizing and killing infected cells. In HIV-infected neonates, NK cell activity is frequently compromised, characterized by reduced cytotoxicity and altered receptor expression.[46] This dysfunction limits the ability to control HIV replication and increases susceptibility to other infections. HIV infection induces chronic immune activation, which can be particularly detrimental in neonates. Persistent activation of the immune system leads to inflammation and tissue damage, exacerbating the depletion of CD4+ T cells and impairing overall immune function. This chronic activation also interferes with the development of trained immunity, reducing the effectiveness of innate immune responses.

HIV-Exposed Uninfected (HEU) infants, while not infected with the virus, still experience significant immunological alterations due to in utero exposure to HIV and ART.[47] These alterations can impact their immune development and susceptibility to infections. Key characteristics of the immune response in HEU neonates include: HEU infants often exhibit distinct cytokine profiles compared to unexposed infants. They may produce higher levels of pro-inflammatory cytokines, such as interleukin-6 (IL-6) and tumor necrosis factor-alpha (TNF-α), and lower levels of anti-inflammatory cytokines like interleukin-10 (IL-10). This imbalance can predispose them to inflammatory conditions and impact their response to infections and vaccinations. The function of various immune cells, including monocytes, macrophages, and dendritic cells, can be altered in HEU infants. These cells may exhibit reduced phagocytic activity,

impaired antigen presentation, and altered cytokine production. Such dysfunctions can compromise the effectiveness of both innate and adaptive immune responses, increasing the risk of infections. HEU infants are at a higher risk of infections, particularly during the early months of life. Studies have shown increased rates of respiratory infections, diarrhea, and other infectious diseases in HEU infants compared to unexposed infants. The underlying mechanisms are multifactorial, involving altered immune responses, exposure to ART, and potential effects of maternal health and nutrition.

Maternal health and the transfer of immune components play a crucial role in shaping the neonatal immune response to HIV. Maternal antibodies, transferred through the placenta and breast milk, provide critical passive immunity to the neonate. However, the quality and quantity of these antibodies can be affected by maternal HIV infection and ART. Additionally, maternal health and nutrition influence the neonatal immune environment, impacting immune development and function. Antiretroviral Therapy (ART) has significantly reduced the rates of vertical transmission of HIV, but its effects on the neonatal immune system are complex. While ART reduces viral load and chronic immune activation, it can also affect the function of immune cells and the development of the neonatal immune system. Understanding the long-term impact of in utero and postnatal exposure to ART on the immune responses of HEU and HIV-infected neonates is crucial for optimizing treatment strategies. Addressing the unique immunological challenges faced by HIV-exposed and infected neonates requires targeted interventions. Enhancing innate immune responses through the use of immune modulators, cytokine therapy, and vaccines designed to induce trained immunity could improve the ability of these infants to combat infections. Additionally, optimizing ART regimens to support immune function and minimize adverse effects is essential for improving health outcomes.[48-51]

Conclusion

The interplay between HIV and the neonatal immune system is a critical area of study, given the significant implications for the health and development of infants born to HIV-positive mothers. HIV-infected neonates face profound immunological challenges, including impaired innate immune functions, NK cell dysfunction, and chronic immune activation. These issues compromise their ability to control infections and respond effectively to vaccinations. HEU infants, although not infected with HIV, still experience altered immune responses due to in utero exposure to the virus and ART. These alterations can lead to a higher susceptibility to infections and inflammatory conditions, highlighting the need for targeted interventions to support their immune health. Maternal factors, including the transfer of antibodies and the effects of ART, play a crucial role in shaping the neonatal immune landscape. Optimizing maternal health and ART regimens can improve outcomes for both HIV-infected and HEU infants.

References

1. 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
2. Obeagu EI, Obeagu, GU. Counting Cells, Shaping Fates: CD4/CD8 Ratios in HIV. EliteJournal of Scientific Research and Review, 2024; 2(1): 37-50

3. Obeagu EI, Obeagu GU. Hematological Changes Following Blood Transfusion in Young Children with Severe Malaria and HIV: A Critical Review. Elite Journal of Laboratory Medicine, 2024; 2(1): 33-45
4. Obeagu EI, Obeagu GU. The Role of Blood Transfusion Strategies in HIV Management: Current Insights and Future Directions. Elite Journal of Medicine, 2024; 2(1):10-22
5. 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.
6. Netea MG. Training innate immunity: the changing concept of immunological memory in innate host defence. European journal of clinical investigation. 2013;43(8):881-884.
7. 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.
8. Viola N, Kimono E, Nuruh N, Obeagu EI. Factors Hindering Elimination of Mother to Child Transmission of HIV Service Uptake among HIV Positive Women at Comboni Hospital Kyamuhunga Bushenyi District. Asian Journal of Dental and Health Sciences. 2023;3(2):7-14.
9. Obeagu EI, Obeagu GU. Transfusion-Related Complications in Children Under 5 with Coexisting HIV and Severe Malaria: A Review. Int. J. Curr. Res. Chem. Pharm. Sci. 2024;11(2):9-19.
10. 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).
11. 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
12. 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.
13. Arikawa S, Rollins N, Newell ML, Becquet R. Mortality risk and associated factors in HIV-exposed, uninfected children. Tropical Medicine & International Health. 2016;21(6):720-734.
14. Brennan AT, Bonawitz R, Gill CJ, Thea DM, Kleinman M, Useem J, Garrison L, Ceccarelli R, Udokwu C, Long L, Fox MP. A meta-analysis assessing all-cause mortality in HIV-exposed uninfected compared with HIV-unexposed uninfected infants and children. Aids. 2016;30(15):2351-2360.
15. Obeagu EI, Anyiam AF, Obeagu GU. Erythropoietin Therapy in HIV-Infected Individuals: A Critical Review. Elite Journal of HIV, 2024; 2(1): 51-64
16. Obeagu EI, Obeagu GU. Strength in Unity: Building Support Networks for HIV Patients in Uganda . Elite Journal of Medicine, 2024; 2(1): 1-16
17. 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
18. 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

Citation: Obeagu EI. HIV and Innate Immune Memory in Neonates. Elite Journal of Immunology, 2024; 2(6): 44-52

19. 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.
20. Obeagu EI, Nweke JO. Neonatal Immune Development in the Context of HIV Infection: A Review. Elite Journal of Immunology. 2024;2(5):29-38.
21. Obeagu EI. Immune Dysregulation in HIV-Positive Neonates: A Review. Elite Journal of Laboratory Medicine. 2024;2(6):49-66.
22. Obeagu EI, Obeagu GU. Maternal Influence on Infant Immunological Responses to HIV: A Review. Elite Journal of Laboratory Medicine. 2024;2(1):46-58.
23. Obeagu EI, Obeagu GU. An update on Early Immunological Markers in HIV-Exposed Infants. Elite Journal of Immunology. 2024;2(6):15-25.
24. Kampmann B, Jones CE. Factors influencing innate immunity and vaccine responses in infancy. Philosophical Transactions of the Royal Society B: Biological Sciences. 2015 Jun 19;370(1671):20140148.
25. Obeagu EI. HIV-Specific T-Cell Responses in Infants: A Review. Elite Journal of Medical Sciences. 2024;2(6):10-23.
26. Diamond MS, Kanneganti TD. Innate immunity: the first line of defense against SARS-CoV-2. Nature immunology. 2022;23(2):165-176.
27. Amarante-Mendes GP, Adjemian S, Branco LM, Zanetti LC, Weinlich R, Bortoluci KR. Pattern recognition receptors and the host cell death molecular machinery. Frontiers in immunology. 2018; 9:2379.
28. Andoniou CE, Andrews DM, Degli-Esposti MA. Natural killer cells in viral infection: more than just killers. Immunological reviews. 2006;214(1):239-250.
29. Mayer LS, Uciechowski P, Meyer S, Schwerdtle T, Rink L, Haase H. Differential impact of zinc deficiency on phagocytosis, oxidative burst, and production of pro-inflammatory cytokines by human monocytes. Metallomics. 2014;6(7):1288-1295.
30. Basha S, Surendran N, Pichichero M. Immune responses in neonates. Expert review of clinical immunology. 2014;10(9):1171-1184.
31. Maródi L. Neonatal innate immunity to infectious agents. Infection and immunity. 2006;74(4):1999-2006.
32. 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
33. 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
34. Obeagu EI. Erythropoietin and the Immune System: Relevance in HIV Management. Elite Journal of Health Science, 2024; 2(3): 23-35
35. 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
36. Obeagu EI, Obeagu GU. Anemia and Erythropoietin: Key Players in HIV Disease Progression. Elite Journal of Haematology, 2024; 2(3): 42-57

Citation: Obeagu EI. HIV and Innate Immune Memory in Neonates. Elite Journal of Immunology, 2024; 2(6): 44-52

37. 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
38. 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
39. Blanco JR, Negredo E, Bernal E, Blanco J. Impact of HIV infection on aging and immune status. Expert Review of Anti-infective Therapy. 2021;19(6):719-731.
40. Olbrich L, Stockdale L, Basu Roy R, Song R, Cicin-Sain L, Whittaker E, Prendergast AJ, Fletcher H, Seddon JA. Understanding the interaction between cytomegalovirus and tuberculosis in children: the way forward. PLoS Pathogens. 2021;17(12): e1010061.
41. Fok ET, Davignon L, Fanucchi S, Mhlanga MM. The lncRNA connection between cellular metabolism and epigenetics in trained immunity. Frontiers in Immunology. 2019; 9:3184.
42. Cuenca AG, Wynn JL, Moldawer LL, Levy O. Role of innate immunity in neonatal infection. American journal of perinatology. 2013;30(02):105-112.
43. Obeagu EI, Obeagu GU. Maternal Influence on Infant Immunological Responses to HIV: A Review. Elite Journal of Laboratory Medicine. 2024;2(1):46-58.
44. Obeagu EI, Obeagu GU. Impact of Maternal Eosinophils on Neonatal Immunity in HIV-Exposed Infants: A Review. Elite Journal of Immunology. 2024;2(3):1-8.
45. Lowenthal ED, Bakeera-Kitaka S, Marukutira T, Chapman J, Goldrath K, Ferrand RA. Perinatally acquired HIV infection in adolescents from sub-Saharan Africa: a review of emerging challenges. The Lancet infectious diseases. 2014;14(7):627-639.
46. Obeagu EI, Chukwu PH. HIV and Natural Killer (NK) Cell Responses in Neonates: A Review. Elite Journal of Immunology. 2024;2(5):39-49.
47. Ruck C, Reikie BA, Marchant A, Kollmann TR, Kakkar F. Linking susceptibility to infectious diseases to immune system abnormalities among HIV-exposed uninfected infants. Frontiers in immunology. 2016; 7:310.
48. Langel SN, Blasi M, Permar SR. Maternal immune protection against infectious diseases. Cell Host & Microbe. 2022 May 11;30(5):660-674.
49. Obeagu EI. Markers of Immune Activation in HIV-Exposed Infants. Elite Journal of Health Science. 2024;2(6):1-4.
50. Obeagu EI, Obeagu GU. Maternal Eosinophilic Responses in HIV-Positive Pregnant Women: Unraveling Immunological Dynamics for Improved Maternal-Fetal Health. Elite Journal of Immunology. 2024;2(1):47-64.
51. Obeagu EI, Obeagu GU. Impact of Breastfeeding on Infant Immune Responses in the Context of HIV. Elite Journal of Nursing and Health Science. 2024;2(4):23-39.