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# Antiretroviral Therapy and Platelet Interactions in HIV Patients: A Review

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## Abstract
Antiretroviral therapy (ART) has transformed HIV infection from a life-threatening disease to a manageable chronic condition, significantly improving patient outcomes. However, HIV-infected individuals on ART often experience alterations in platelet function and dynamics, posing challenges in clinical management. Thrombocytopenia, platelet hyperactivation, and increased thrombotic risk are prevalent in this population, necessitating a comprehensive understanding of the mechanisms underlying these platelet alterations and their clinical implications. Chronic immune activation and inflammation, hallmark features of HIV infection, persist despite effective viral suppression with ART. Elevated levels of pro-inflammatory cytokines contribute to platelet activation and turnover, leading to thrombocytopenia and platelet dysfunction. Furthermore, ART drugs themselves can directly influence platelet function, with protease inhibitors being associated with increased platelet activation and aggregation. Clinicians must carefully balance the benefits of ART with its potential adverse effects on platelet dynamics, tailoring treatment regimens to individual patient profiles and risk factors. Personalized approaches to management, informed by a thorough understanding of the underlying mechanisms, are crucial for optimizing outcomes in this population. Ongoing research efforts aimed at elucidating the long-term effects of ART on platelet function and developing targeted interventions hold promise for improving the health outcomes and quality of life for individuals living with HIV.

***Keywords:*** *Antiretroviral Therapy, Platelets, HIV, Thrombocytopenia, Platelet Dysfunction, Immune Activation, Inflammation, Cardiovascular Risk*

## Introduction
Antiretroviral therapy (ART) stands as a cornerstone in the management of HIV infection, marking a transformative shift from a once-debilitating disease to a chronic condition. ART's effectiveness lies in its ability to suppress viral replication, thereby reducing immune system deterioration and averting AIDS-related complications. However, despite the remarkable advancements achieved with ART, HIV-infected individuals continue to grapple with a spectrum of health challenges,

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among which alterations in platelet function and dynamics emerge as significant concerns. Platelets, classically acknowledged for their role in hemostasis, are increasingly recognized for their multifaceted involvement in immune responses and inflammation, processes that are intricately intertwined with HIV pathogenesis and its treatment.[1-5] A prevailing concern in HIV-infected individuals, both prior to and during ART, is thrombocytopenia—a condition characterized by abnormally low platelet counts. The etiology of HIV-associated thrombocytopenia is complex, involving multifactorial mechanisms such as direct viral effects on megakaryocytes, increased platelet destruction, and impaired platelet production. While ART initiation typically leads to an improvement in platelet counts, the extent of recovery varies widely among individuals and is influenced by factors including the ART regimen employed and baseline platelet count. Beyond thrombocytopenia, HIV infection and its treatment are associated with platelet hyperactivation, predisposing individuals to a prothrombotic state and heightened cardiovascular risks.[6-10]

The mechanisms underlying platelet alterations in ART-treated HIV patients are multifaceted. Chronic immune activation and persistent inflammation, characteristic features of HIV infection, persist despite effective viral suppression with ART. These processes perpetuate platelet activation and turnover, contributing to thrombocytopenia and dysfunctional platelet responses. Moreover, ART drugs themselves can directly influence platelet function, with certain drug classes, such as protease inhibitors, being associated with heightened platelet activation and aggregation.[11-12] The platelet abnormalities observed in ART-treated HIV patients carry significant clinical implications. Thrombocytopenia poses a risk for bleeding complications, necessitating vigilant monitoring and management strategies. Concurrently, the heightened thrombotic risk associated with platelet hyperactivation underscores the importance of cardiovascular risk assessment and management in this population. Personalized treatment approaches, guided by a nuanced understanding of individual patient profiles and risk factors, are paramount for optimizing outcomes. Furthermore, ongoing research endeavors aimed at delineating the long-term effects of ART on platelet dynamics and developing targeted interventions hold promise for advancing patient care and improving quality of life for individuals living with HIV.[13-17]

**Mechanisms of Platelet Alterations**

Platelet alterations in HIV-infected individuals receiving antiretroviral therapy (ART) represent a complex interplay of viral, immunological, and pharmacological factors.

- **Chronic Immune Activation and Inflammation**: Persistent immune activation, a hallmark of HIV infection, perpetuates systemic inflammation even in the presence of effective ART. Elevated levels of pro-inflammatory cytokines such as interleukin-6 (IL-6) and tumor necrosis factor-alpha (TNF-α) contribute to increased platelet activation and turnover. This chronic stimulation of platelets leads to a state of hyperreactivity, predisposing individuals to thrombocytopenia and thrombotic events. Furthermore,

immune dysregulation can result in the production of autoantibodies against platelet glycoproteins, leading to immune-mediated platelet destruction.[18-20]

- **Direct Effects of HIV and ART on Megakaryocytes**: HIV can directly infect bone marrow precursor cells, including megakaryocytes, leading to impaired platelet production. Although ART effectively suppresses viral replication in peripheral blood, residual viral presence in sanctuary sites such as the bone marrow can continue to affect megakaryocyte function. Additionally, certain ART drugs, particularly nucleoside reverse transcriptase inhibitors (NRTIs), can induce mitochondrial toxicity, impairing megakaryocyte proliferation and platelet production.[21-22]
- **ART Drug-Specific Effects**: Different classes of ART drugs exert varying effects on platelet function. Protease inhibitors, such as ritonavir and lopinavir, have been associated with increased platelet activation and aggregation. These effects may be mediated through alterations in lipid metabolism, insulin resistance, and endothelial dysfunction. In contrast, integrase strand transfer inhibitors (INSTIs) and non-nucleoside reverse transcriptase inhibitors (NNRTIs) generally have a more neutral effect on platelet function. Understanding these drug-specific effects is crucial for optimizing ART regimens to minimize adverse hematological outcomes.[23-24]
- **Thrombotic Risk and Cardiovascular Complications**: Platelet hyperactivation and a prothrombotic state in HIV-infected individuals on ART contribute to an increased risk of cardiovascular events. Endothelial dysfunction, driven by chronic inflammation and immune dysregulation, further exacerbates thrombotic tendencies. ART drugs, particularly protease inhibitors, may exacerbate these cardiovascular risks through their effects on lipid metabolism and endothelial function. Consequently, HIV-infected individuals face a heightened risk of myocardial infarction, stroke, and venous thromboembolism, underscoring the importance of cardiovascular risk assessment and management in this population.[24-28]

**Clinical Implications**

The platelet alterations observed in HIV-infected individuals receiving antiretroviral therapy (ART) have significant clinical implications, necessitating tailored management strategies to optimize patient outcomes.

- **Thrombocytopenia Management**: Thrombocytopenia, characterized by abnormally low platelet counts, poses a risk for bleeding complications in HIV patients on ART. Regular monitoring of platelet counts is essential to detect thrombocytopenia early. Management strategies may include addressing underlying causes such as opportunistic infections or medication side effects. In severe cases, interventions such as corticosteroids, intravenous immunoglobulin (IVIG), or platelet transfusions may be warranted to raise platelet counts and prevent bleeding complications. Clinicians must carefully weigh the risks and benefits of these interventions, considering the individual patient's clinical status and comorbidities.[29-32]

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- **Cardiovascular Risk Assessment and Management**: Platelet hyperactivation and a prothrombotic state in HIV-infected individuals increase the risk of cardiovascular events, including myocardial infarction and stroke. Therefore, comprehensive cardiovascular risk assessment and management are essential components of HIV care. This includes monitoring lipid profiles, blood pressure, and inflammatory markers, and initiating lifestyle modifications such as smoking cessation, regular exercise, and dietary changes. Pharmacological interventions, such as statins or antiplatelet agents, may be indicated to mitigate cardiovascular risks in high-risk individuals. Clinicians should integrate cardiovascular risk assessment into routine HIV care to optimize cardiovascular outcomes in this population.[33-35]
- **Optimization of ART Regimens**: The choice of ART regimen can influence platelet function and hematological outcomes in HIV-infected individuals. Clinicians should carefully consider the potential hematological effects of different ART drugs when selecting treatment regimens. Protease inhibitors, known to increase platelet activation and aggregation, may be avoided in patients with pre-existing cardiovascular risks or platelet abnormalities. Instead, integrase strand transfer inhibitors (INSTIs) or non-nucleoside reverse transcriptase inhibitors (NNRTIs) may be preferred due to their more neutral effect on platelet function. Personalized ART regimens tailored to individual patient profiles can help minimize adverse hematological effects while maintaining effective viral suppression.[36-40]
- **Regular Monitoring and Follow-Up**: Close monitoring and regular follow-up are crucial components of HIV care, particularly in individuals with known hematological abnormalities or cardiovascular risks. Regular assessment of platelet counts, cardiovascular risk factors, and medication adherence can facilitate early detection and intervention for complications. Additionally, patient education and counseling on lifestyle modifications, medication adherence, and the importance of regular follow-up are essential for empowering patients to actively engage in their healthcare and minimize the risk of complications.[41]
- **Future Research and Clinical Guidelines**: Continued research efforts are needed to further elucidate the mechanisms underlying platelet alterations in HIV-infected individuals and develop evidence-based clinical guidelines for their management. Longitudinal studies evaluating the long-term effects of ART on platelet function and cardiovascular outcomes are warranted to inform optimal treatment strategies. Collaboration between hematologists, cardiologists, and HIV specialists is essential to develop comprehensive care plans that address both hematological and cardiovascular risks in this population. By optimizing clinical management strategies, clinicians can improve the quality of life and long-term outcomes for HIV-infected individuals receiving ART.[40]

## Conclusion

In conclusion, the intricate interplay between HIV infection, antiretroviral therapy (ART), and platelet dynamics underscores the complexity of managing hematological and cardiovascular complications in this population. Thrombocytopenia, platelet hyperactivation, and increased thrombotic risk represent significant challenges in clinical practice, necessitating tailored

management strategies to optimize patient outcomes. The persistence of chronic immune activation and inflammation despite viral suppression with ART underscores the need for comprehensive cardiovascular risk assessment and management in HIV care. Additionally, the choice of ART regimen plays a crucial role in influencing platelet function and hematological outcomes, highlighting the importance of personalized treatment approaches based on individual patient profiles and risk factors.

**References**

1. Russell S, Seeley J. The transition to living with HIV as a chronic condition in rural Uganda: Working to create order and control when on antiretroviral therapy. Social science & medicine. 2010;70(3):375-382.
2. Vella S, Schwartländer B, Sow SP, Eholie SP, Murphy RL. The history of antiretroviral therapy and of its implementation in resource-limited areas of the world. Aids. 2012;26(10):1231-1241.
3. Obeagu EI, Obeagu GU, Paul-Chima UO. Stigma Associated With HIV. AIDS: A Review. Newport International Journal of Public Health and Pharmacy (Nijpp). 2023;3(2):64-67.
4. Alum EU, Obeagu EI, Ugwu OP, Aja PM, Okon MB. HIV infection and cardiovascular diseases: the obnoxious duos. Newport International Journal of Research in Medical Sciences (NIJRMS). 2023;3(2):95-99.
5. 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
6. Marchionatti A, Parisi MM. Anemia and thrombocytopenia in people living with HIV/AIDS: a narrative literature review. International Health. 2021 Mar;13(2):98-109.
7. Vishnu P, Aboulafia DM. Haematological manifestations of human immune deficiency virus infection. British journal of haematology. 2015 Dec;171(5):695-709.
8. Ifeanyi OE, Favour AA, Prayer NN. Updates on Human Immunodeficiency Virus and Platelets. Int. J. Adv. Res. Biol. Sci. 2020;7(6):1-7.
9. Miguez-Burbano MJ, Jackson Jr J, Hadrigan S. Thrombocytopenia in HIV disease: clinical relevance, physiopathology and management. Current Medicinal Chemistry-Cardiovascular & Hematological Agents. 2005;3(4):365-376.
10. 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 J Dental Health Sci. 2024; 30];3(2):7-14. http://ajdhs.com/index.php/journal/article/view/39
11. 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.
12. 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
13. 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

**Citation**: Ezeonwumelu JOC, Obeagu EI. Antiretroviral Therapy and Platelet Interactions in HIV Patients: A Review. Elite Journal of Health Science, 2024; 2(5): 30-36

14. 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.
15. 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).
16. Marchionatti A, Parisi MM. Anemia and thrombocytopenia in people living with HIV/AIDS: a narrative literature review. International Health. 2021;13(2):98-109.
17. Younas M, Psomas C, Reynes J, Corbeau P. Immune activation in the course of HIV-1 infection: causes, phenotypes and persistence under therapy. HIV medicine. 2016;17(2):89-105.
18. Zicari S, Sessa L, Cotugno N, Ruggiero A, Morrocchi E, Concato C, Rocca S, Zangari P, Manno EC, Palma P. Immune activation, inflammation, and non-AIDS co-morbidities in HIV-infected patients under long-term ART. Viruses. 2019;11(3):200.
19. Madzime M, Rossouw TM, Theron AJ, Anderson R, Steel HC. Interactions of HIV and antiretroviral therapy with neutrophils and platelets. Frontiers in immunology. 2021; 12:634386.
20. Bluestein D, Chandran KB, Manning KB. Towards non-thrombogenic performance of blood recirculating devices. Annals of biomedical engineering. 2010; 38:1236-56.
21. Akinosoglou K, Kolosaka M, Schinas G, Delastic AL, Antonopoulou S, Perperis A, Marangos M, Mouzaki A, Gogos C. Association of Antiretroviral Therapy with Platelet Function and Systemic Inflammatory Response in People Living with HIV: A Cross-Sectional Study. Microorganisms. 2023;11(4):958.
22. 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.
23. Obeagu EI, Obeagu GU. Strength in Unity: Building Support Networks for HIV Patients in Uganda. Elite Journal of Medicine. 2024;2(1):1-6.
24. Obeagu EI, GU EE. Understanding the Intersection of Highly Active Antiretroviral Therapy and Platelets in HIV Patients: A Review. Elite Journal of Haematology, 2024; 2 (3).:111-7.
25. Baker JV, Brummel-Ziedins K, Neuhaus J, Duprez D, Cummins N, Dalmau D, DeHovitz J, Lehmann C, Sullivan A, Woolley I, Kuller L. HIV replication alters the composition of extrinsic pathway coagulation factors and increases thrombin generation. Journal of the American Heart Association. 2013;2(4): e000264.
26. Obeagu EI, Obeagu GU. ART and Platelet Dynamics: Assessing Implications for HIV Patient Care. Elite Journal of Haematology. 2024;2(4):68-85.
27. 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.
28. Obeagu EI, Obeagu GU. Platelet Aberrations in HIV Patients: Assessing Impacts of ART. Elite Journal of Haematology. 2024;2(3):10-24.
29. Obeagu EI, EE G. Understanding the Intersection of Highly Active Antiretroviral Therapy and Platelets in HIV Patients: A Review. Elite Journal of Haematology. 2024;2(3):111-7.

**Citation**: Ezeonwumelu JOC, Obeagu EI. Antiretroviral Therapy and Platelet Interactions in HIV Patients: A Review. Elite Journal of Health Science, 2024; 2(5): 30-36

30. Obeagu EI, Obeagu GU. Platelet Dysfunction in HIV Patients: Assessing ART Risks. Elite Journal of Scientific Research and Review. 2024;2(1):1-6.
31. Obeagu EI, Obeagu GU. Platelet Dysfunction in HIV Patients: Assessing ART Risks. Elite Journal of Scientific Research and Review. 2024;2(1):1-6.
32. Tripathi AK, Misra R, Kalra P, Gupta N, Ahmad R. Bone marrow abnormalities in HIV disease. JAPI. 2005; 53:705-10.
33. Shenkman B, Rosenberg N, Einav Y. Platelet autoantibodies. In Autoantibodies 2014: 519-525. Elsevier.
34. Talargia F, Getacher L. Thrombocytopenia and associated factors among HIV infected patients in Pre-and post-anti-retroviral therapy, North East Ethiopia. Journal of Blood Medicine. 2021:741-748.
35. Henning RJ, Greene JN. The epidemiology, mechanisms, diagnosis and treatment of cardiovascular disease in adult patients with HIV. American journal of cardiovascular disease. 2023;13(2):101.
36. Goedel A, Müller S, Schwerdtfeger C, Zink A, Noe S, Bongiovanni D, Haller B, Spinner CD, Bernlochner I. Influence of antiretroviral therapy and cardiovascular disease on the immature platelet fraction in patients living with HIV. Platelets. 2020;31(6):756-762.
37. Obeagu EI, Obeagu GU. ART and Platelet Dynamics: Assessing Implications for HIV Patient Care. Elite Journal of Haematology. 2024;2(4):68-85.
38. Obeagu EI, Obeagu GU. Platelet Aberrations in HIV Patients: Assessing Impacts of ART. Elite Journal of Haematology. 2024;2(3):10-24.
39. Obeagu EI, Obeagu GU. Platelet Dysfunction in HIV Patients: Assessing ART Risks. Elite Journal of Scientific Research and Review. 2024;2(1):1-6.
40. Shen Y, Liu T, Chen J, Li X, Liu L, Shen J, Wang J, Zhang R, Sun M, Wang Z, Song W. Harnessing artificial intelligence to optimize long-term maintenance dosing for antiretroviral-naive adults with HIV-1 infection. Advanced Therapeutics. 2020 Apr;3(4):1900114.
41. Obeagu EI, Obeagu GU. Platelet index ratios in HIV: Emerging biomarkers for immune health and disease management. Medicine. 2024 Mar 22;103(12):e37576.

**Citation**: Ezeonwumelu JOC, Obeagu EI. Antiretroviral Therapy and Platelet Interactions in HIV Patients: A Review. Elite Journal of Health Science, 2024; 2(5): 30-36