# Understanding the Impact of Blood Transfusion on Erythropoiesis in Pediatric Severe Malaria Cases with HIV: A Review



Understanding the Impact of Blood Transfusion on Erythropoiesis in Pediatric Severe Malaria Cases with HIV: A Review

\*Emmanuel Ifeanyi Obeagu

Department of Medical Laboratory Science, Kampala International University, Uganda

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

#### **Abstract**

Pediatric severe malaria cases complicated by HIV co-infection present a multifaceted clinical scenario that demands a comprehensive understanding of disease pathophysiology and treatment implications. This review delves into the intricate interplay between blood transfusion and erythropoiesis in this vulnerable population. Severe malaria induces hemolysis and anemia, exacerbating tissue hypoxia, while HIV compromises immune function and increases susceptibility to infections and anemia. The combined effects of these diseases pose significant challenges in managing pediatric patients, necessitating tailored approaches to transfusion therapy and erythropoietic support. While transfusion remains a cornerstone intervention to mitigate anemia and improve tissue oxygenation, its risks, including transfusion-transmitted infections and iron overload, must be carefully weighed against potential benefits. Moreover, repeated transfusions may disrupt erythropoietic regulation, exacerbating anemia and complicating treatment strategies in this vulnerable population. Thus, individualized transfusion thresholds and adjunctive therapies targeting erythropoiesis may offer promising avenues to enhance patient care and mitigate transfusion-related risks.

Keywords: Blood Transfusion, Erythropoiesis, Pediatric, Severe Malaria, HIV

## Introduction

Pediatric severe malaria, a life-threatening complication of Plasmodium falciparum infection, remains a significant global health concern, particularly in regions with high malaria endemicity. The clinical manifestations of severe malaria encompass a spectrum of complications, including cerebral malaria, severe anemia, respiratory distress, and metabolic acidosis, posing substantial challenges in management. Compounding this challenge is the concurrent presence of HIV infection in pediatric populations, which not only increases the risk of malaria-related morbidity and mortality but also introduces additional complexities in treatment approaches. As such, understanding the intricate interplay between severe malaria, HIV, and therapeutic interventions like blood transfusion is imperative for optimizing clinical outcomes in this vulnerable patient population. <sup>1-5</sup> Severe malaria-induced anemia, characterized by hemolysis, dyserythropoiesis, and reduced red blood cell survival, significantly contributes to morbidity and mortality, particularly in children under five years of age. The pathophysiology of severe malaria-related anemia involves the sequestration of infected erythrocytes in the microvasculature, leading to impaired microcirculatory flow, tissue hypoxia, and subsequent organ dysfunction. In pediatric patients with HIV, the impact of severe malaria-induced anemia is compounded by the immunosuppressive effects of HIV infection, which heighten susceptibility to infections and exacerbate erythropoietic dysfunction. Consequently, managing anemia in pediatric severe malaria cases with HIV requires a nuanced understanding of disease pathogenesis and tailored therapeutic interventions. <sup>6-13</sup>

Blood transfusion remains a cornerstone intervention in the management of severe anemia in pediatric malaria cases, aiming to improve tissue oxygenation, reverse end-organ damage, and prevent mortality. However, the decision to transfuse must be carefully weighed against the risks transfusion-related complications, including transfusion-transmitted of infections, alloimmunization, and hemolytic reactions. In pediatric patients with HIV, these risks are further compounded by the potential for disease progression and immune dysregulation, necessitating a cautious approach to transfusion therapy. Moreover, the impact of blood transfusion on erythropoiesis in the context of severe malaria and HIV co-infection remains poorly understood, warranting further investigation to inform evidence-based clinical practice. 14-20 While blood transfusion is essential for correcting severe anemia and improving clinical outcomes in pediatric severe malaria cases, its effects on erythropoiesis are complex and multifaceted. Transfusionrelated alterations in iron metabolism, erythropoietin regulation, and bone marrow function may impact long-term erythropoietic capacity and contribute to the persistence of anemia beyond the acute phase of illness. In pediatric patients with HIV, the dysregulation of erythropoiesis resulting from viral infection and immune dysfunction may further exacerbate transfusion-related complications and complicate treatment strategies. Thus, elucidating the impact of blood transfusion on erythropoiesis in pediatric severe malaria cases with HIV is essential for optimizing transfusion practices and improving long-term clinical outcomes. <sup>21-25</sup> The aim of this review is to critically evaluate existing literature on the impact of blood transfusion on erythropoiesis in pediatric severe malaria cases with HIV co-infection.

# Pathophysiology of Severe Malaria and HIV

The pathophysiology of severe malaria and HIV intertwines in a complex manner, posing significant challenges in clinical management, particularly in pediatric populations. Severe malaria, primarily caused by Plasmodium falciparum, manifests with a myriad of complications, including cerebral malaria, severe anemia, respiratory distress, and metabolic acidosis. The hallmark of severe malaria is the sequestration of infected erythrocytes in the microvasculature, particularly in the brain, leading to impaired microcirculatory flow and tissue hypoxia. This sequestration, along with the destruction of infected erythrocytes, contributes to the pathogenesis of severe anemia, a common and life-threatening complication of severe malaria. Additionally, the release of pro-inflammatory cytokines and the activation of endothelial cells further exacerbate tissue injury and organ dysfunction. <sup>26-30</sup> Concurrent with severe malaria, HIV infection introduces a layer of complexity due to its immunosuppressive effects and impact on erythropoiesis. HIV targets CD4+ T lymphocytes, macrophages, and dendritic cells, leading to systemic immune dysregulation and increased susceptibility to opportunistic infections. In pediatric patients, HIVassociated immunosuppression can heighten the severity of malaria and exacerbate anemia through mechanisms such as reduced erythropoietin production, impaired erythrocyte maturation, and dysregulated iron metabolism. Furthermore, HIV-related complications, including HIV-associated nephropathy and opportunistic infections such as tuberculosis, can contribute to anemia and worsen clinical outcomes in severe malaria cases co-infected with HIV. 31-36 The interaction between severe malaria and HIV creates a vicious cycle of immune dysregulation, erythropoietic dysfunction, and organ damage, leading to increased morbidity and mortality in affected pediatric patients.<sup>37</sup> The synergistic effects of these two diseases exacerbate anemia, impair tissue oxygenation, and compromise the body's ability to mount an effective immune response.<sup>38</sup> Moreover, the complexities introduced by HIV, including the potential for drug interactions and treatment-related complications, further complicate clinical management. Therefore, a comprehensive understanding of the pathophysiology of severe malaria and HIV co-infection is essential for devising effective treatment strategies that address the unique needs of pediatric patients in resource-limited settings.

### **Impact of Blood Transfusion on Erythropoiesis**

The impact of blood transfusion on erythropoiesis, particularly in the context of severe malaria and HIV co-infection in pediatric patients, is a topic of considerable importance and complexity.<sup>39</sup> Blood transfusion is a vital intervention aimed at correcting severe anemia, improving tissue oxygenation, and preventing mortality in critically ill patients. However, the effects of transfusion on erythropoiesis extend beyond the immediate correction of anemia and may have implications for long-term hematologic outcomes. In the acute phase, blood transfusion provides an immediate source of red blood cells, restoring oxygen-carrying capacity and alleviating tissue hypoxia.<sup>40</sup> This rapid correction of anemia can be life-saving, particularly in pediatric severe malaria cases where Citation: Obeagu EI. Understanding the Impact of Blood Transfusion on Erythropoiesis in Pediatric Severe Malaria Cases with HIV: A Review. *Elite Journal of Haematology*, 2024; 2(5): 147-154

tissue oxygenation is compromised due to microvascular sequestration of infected erythrocytes. However, the transfusion of allogeneic blood introduces exogenous erythrocytes into the recipient's circulation, which may elicit immune responses and lead to transfusion-related complications such as alloimmunization, hemolytic reactions, and transfusion-transmitted infections. Furthermore, the impact of blood transfusion on erythropoiesis extends beyond the acute phase, with potential implications for long-term hematologic outcomes. Repeated transfusions may disrupt endogenous erythropoietin production, leading to erythropoietin resistance and impaired erythrocyte maturation.<sup>41</sup> Additionally, transfusion-related iron overload may suppress endogenous erythropoiesis by inhibiting erythropoietin production and impairing iron utilization. Consequently, pediatric patients with severe malaria and HIV co-infection who require frequent transfusions may be at increased risk of developing transfusion-dependent anemia and iron overload, further complicating clinical management and long-term outcomes. Moreover, the interplay between blood transfusion and erythropoiesis in the context of severe malaria and HIV co-infection is influenced by various factors, including the patient's immune status, nutritional status, and underlying hematologic disorders. Pediatric patients with HIV may exhibit dysregulated erythropoiesis due to HIV-associated immune dysfunction, opportunistic infections, and antiretroviral therapy-related toxicities. Similarly, severe malaria-induced anemia may exacerbate erythropoietic dysfunction and increase the likelihood of transfusion dependence in affected patients. Therefore, individualized transfusion strategies, tailored to the patient's specific clinical and hematologic profile, are essential for optimizing erythropoietic responses and minimizing transfusion-related risks in pediatric severe malaria cases with HIV co-infection. 42-44

## **Implications for Pediatric Patients**

The implications of blood transfusion on erythropoiesis in pediatric severe malaria cases with HIV co-infection are multifaceted and require careful consideration to optimize clinical outcomes while minimizing transfusion-related risks. <sup>45</sup> Pediatric patients with severe malaria and HIV co-infection present unique challenges due to the complex interplay between disease pathophysiology, immune status, and erythropoietic function. Therefore, tailoring transfusion strategies to the individual needs of each patient is essential to ensure effective management and mitigate adverse outcomes. One of the primary implications for pediatric patients is the need for individualized transfusion thresholds that balance the benefits of correcting severe anemia with the risks of transfusion-related complications. While blood transfusion can rapidly improve tissue oxygenation and prevent mortality in critically ill patients, indiscriminate transfusion practices may exacerbate transfusion-related risks, such as alloimmunization, transfusion-transmitted infections, and iron overload. Therefore, establishing evidence-based transfusion thresholds based on the patient's clinical status, hemoglobin level, and underlying comorbidities is essential to optimize transfusion practices and improve patient outcomes.

Furthermore, pediatric patients with severe malaria and HIV co-infection may require adjunctive therapies targeting erythropoiesis to mitigate transfusion-dependent anemia and optimize long-term hematologic outcomes. Iron supplementation, erythropoietin-stimulating agents, and nutritional interventions may play a crucial role in supporting endogenous erythropoiesis and reducing transfusion requirements in affected patients. Additionally, close monitoring of iron status, erythropoietic parameters, and transfusion-related complications is essential to identify patients at risk of developing transfusion-dependent anemia and implement timely interventions to prevent long-term sequelae. Moreover, the implications of blood transfusion on erythropoiesis extend beyond the acute phase of illness and may have long-term implications for pediatric patients with severe malaria and HIV co-infection. Repeated transfusions may lead to transfusion-dependent anemia, iron overload, and erythropoietic dysfunction, further complicating clinical management and increasing the risk of morbidity and mortality. Therefore, a multidisciplinary approach involving pediatricians, hematologists, infectious disease specialists, and transfusion medicine experts is essential to develop comprehensive management strategies that address the unique needs of pediatric patients in resource-limited settings.

#### **Conclusion**

The management of pediatric severe malaria cases with HIV co-infection necessitates a nuanced understanding of the implications of blood transfusion on erythropoiesis. Optimizing transfusion practices requires careful consideration of transfusion thresholds, transfusion-related risks, and the potential for long-term hematologic sequelae. Individualized transfusion thresholds should be established based on the patient's clinical status, hemoglobin level, and underlying comorbidities, with a focus on minimizing transfusion-related risks while ensuring effective correction of severe anemia. Additionally, adjunctive therapies targeting erythropoiesis, such as iron supplementation and erythropoietin-stimulating agents, may play a crucial role in reducing transfusion requirements and improving long-term hematologic outcomes in affected patients.

#### References

- 1. Manning L, Laman M, Davis WA, Davis TM. Clinical features and outcome in children with severe Plasmodium falciparum malaria: a meta-analysis. PLoS One. 2014;9(2):e86737.
- 2. Patel H, Dunican C, Cunnington AJ. Predictors of outcome in childhood Plasmodium falciparum malaria. Virulence. 2020;11(1):199-221.
- 3. 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.
- 4. 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.

- 5. 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.
- 6. Balaji SN, Deshmukh R, Trivedi V. Severe malaria: Biology, clinical manifestation, pathogenesis and consequences. Journal of Vector Borne Diseases. 2020;57(1):1-3.
- 7. White NJ. Anaemia and malaria. Malaria journal. 2018;17(1):371.
- 8. Perkins DJ, Were T, Davenport GC, Kempaiah P, Hittner JB, Ong'echa JM. Severe malarial anemia: innate immunity and pathogenesis. International journal of biological sciences. 2011;7(9):1427.
- 9. Obeagu EI, Obeagu GU, Chukwueze CM, Ikpenwa JN, Ramos GF. EVALUATION OF PROTEIN C, PROTEIN S AND FIBRINOGEN OF PREGNANT WOMEN WITH MALARIA IN OWERRI METROPOLIS. Madonna University journal of Medicine and Health Sciences ISSN: 2814-3035. 2022;2(2):1-9.
- 10. Obeagu EI, Ibeh NC, Nwobodo HA, Ochei KC, Iwegbulam CP. Haematological indices of malaria patients coinfected with HIV in Umuahia. Int. J. Curr. Res. Med. Sci. 2017;3(5):100-104.
- 11. Opeyemi AA, Obeagu EI. Regulations of malaria in children with human immunodeficiency virus infection: A review. Medicine. 2023;102(46): e36166.
- 12. 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.
- 13. 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 [Internet]. 2023;3(2):7-14. <a href="http://ajdhs.com/index.php/journal/article/view/39">http://ajdhs.com/index.php/journal/article/view/39</a>
- 14. Tzounakas VL, Valsami SI, Kriebardis AG, Papassideri IS, Seghatchian J, Antonelou MH. Red cell transfusion in paediatric patients with thalassaemia and sickle cell disease: current status, challenges and perspectives. Transfusion and apheresis science. 2018 Jun 1:57(3):347-57.
- 15. Singh U. Hematological Diseases and Syndromes in the Neonate: Haemoglobin, Haemoglobinopathies, and Oxygen Therapy. InClinical Anesthesia for the Newborn and the Neonate 2023; 291-313. Singapore: Springer Nature Singapore.
- 16. 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
- 17. 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
- 18. Obeagu EI, Okwuanaso CB, Edoho SH, Obeagu GU. Under-nutrition among HIV-exposed Uninfected Children: A Review of African Perspective. Madonna University journal of Medicine and Health Sciences. 2022;2(3):120-127.
- 19. Obeagu EI. A Review of Challenges and Coping Strategies Faced by HIV/AIDS Discordant Couples. Madonna University journal of Medicine and Health Sciences. 2023

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;3(1):7-12. https://madonnauniversity.edu.ng/journals/index.php/medicine/article/view/91.

- 20. Obeagu EI, Obeagu GU. An update on premalignant cervical lesions and cervical cancer screening services among HIV positive women. J Pub Health Nutri. 2023; 6 (2). 2023; 141:1-2. <a href="links/63e538ed64252375639dd0df/An-update-on-premalignant-cervical-lesions-and-cervical-cancer-screening-services-among-HIV-positive-women.pdf">links/63e538ed64252375639dd0df/An-update-on-premalignant-cervical-lesions-and-cervical-cancer-screening-services-among-HIV-positive-women.pdf</a>.
- 21. 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.
- 22. 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.
- 23. 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.
- 24. Obeagu EI, Obeagu GU. Advances in Understanding the Impact of Blood Transfusion on Anemia Resolution in HIV-Positive Children with Severe Malaria: A Comprehensive Review. Elite Journal of Haematology. 2024;2(1):26-41.
- 25. Obeagu EI, Babar Q, Obeagu GU. Allergic blood Transfusion reaction: A Review. Int. J. Curr. Res. Med. Sci. 2021;7(5):25-33.
- 26. Opeyemi AA, Obeagu EI. Regulations of malaria in children with human immunodeficiency virus infection: A review. Medicine. 2023;102(46): e36166.
- 27. Obeagu EI, Obeagu GU, Ukibe NR, Oyebadejo SA. Anemia, iron, and HIV: decoding the interconnected pathways: A review. Medicine. 2024;103(2): e36937.
- 28. Obeagu EI, Obeagu GU. Tackling childhood anemia in malaria zones: comprehensive strategies, challenges, and future directions. Academia Medicine. 2024; 1:1-6.
- 29. Nhampossa T, Sigaúque B, Machevo S, Macete E, Alonso P, Bassat Q, Menéndez C, Fumadó V. Severe malnutrition among children under the age of 5 years admitted to a rural district hospital in southern Mozambique. Public health nutrition. 2013;16(9):1565-1574.
- 30. Wasserheit JN, Holmes KK. Reproductive tract infections: challenges for international health policy, programs, and research. InReproductive tract infections: Global impact and priorities for women's reproductive health 1992; 7-33. Boston, MA: Springer US.
- 31. 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.
- 32. Obeagu EI, Obeagu GU. Advances in Understanding the Impact of Blood Transfusion on Anemia Resolution in HIV-Positive Children with Severe Malaria: A Comprehensive Review. Elite Journal of Haematology. 2024;2(1):26-41.
- 33. Obeagu EI, Obeagu GU. Synergistic Effects of Blood Transfusion and HIV in Children Under 5 Years with Severe Malaria: A Review. Elite Journal of HIV. 2024;2(1):31-50.

Elite Journal of Haematology. Volume 2 issue 5(2024), Pp. 147-154 https://epjournals.com/journals/EJH

- 34. Obeagu EI, Obeagu GU. Hematologic Considerations in Breast Cancer Patients with HIV: Insights into Blood Transfusion Strategies. Elite Journal of Health Science. 2024;2(2):20-35.
- 35. Obeagu EI, Obeagu GU. The Nexus Between Obesity and Leukemia Progression in HIV-Positive Individuals: A Review. Elite Journal of Haematology. 2024;2(4):180-98.
- 36. Akoolo L, Rocha SC, Parveen N. Protozoan co-infections and parasite influence on the efficacy of vaccines against bacterial and viral pathogens. Frontiers in Microbiology. 2022; 13:1020029.
- 37. Obeagu EI, Obeagu GU. Anemia and Malaria: Twin Troubles in Pediatric Health. Elite Journal of Health Science. 2024;2(3):36-43.
- 38. Wintergerst ES, Maggini S, Hornig DH. Contribution of selected vitamins and trace elements to immune function. Annals of nutrition and metabolism. 2007;51(4):301-323.
- 39. Haldar K, Mohandas N. Malaria, erythrocytic infection, and anemia. ASH Education Program Book. 2009;2009(1):87-93.
- 40. Tsai AG, Hofmann A, Cabrales P, Intaglietta M. Perfusion vs. oxygen delivery in transfusion with "fresh" and "old" red blood cells: the experimental evidence. Transfusion and apheresis science. 2010;43(1):69-78.
- 41. Jelkmann W. Erythropoietin: structure, control of production, and function. Physiological reviews. 1992;72(2):449-489.
- 42. Ezeoru VC, Enweani IB, Ochiabuto O, Nwachukwu AC, Ogbonna US, Obeagu EI. Prevalence of Malaria with Anaemia and HIV status in women of reproductive age in Onitsha, Nigeria. Journal of Pharmaceutical Research International. 2021;33(4):10-19.
- 43. Omo-Emmanuel UK, Chinedum OK, Obeagu EI. Evaluation of laboratory logistics management information system in HIV/AIDS comprehensive health facilities in Bayelsa State, Nigeria. Int J Curr Res Med Sci. 2017;3(1): 21-38.DOI: 10.22192/ijcrms.2017.03.01.004
- 44. Obeagu EI, Obeagu GU. An update on survival of people living with HIV in Nigeria. J Pub Health Nutri. 2022; 5 (6). 2022;129. <a href="links/645b4bfcf3512f1cc5885784/An-update-on-survival-of-people-living-with-HIV-in-Nigeria.pdf">links/645b4bfcf3512f1cc5885784/An-update-on-survival-of-people-living-with-HIV-in-Nigeria.pdf</a>.
- 45. Obeagu EI, Obeagu GU. Advances in Understanding the Impact of Blood Transfusion on Anemia Resolution in HIV-Positive Children with Severe Malaria: A Comprehensive Review. Elite Journal of Haematology. 2024;2(1):26-41.
- 46. Pradesh A. 4th ISTM Annual Conference, TRANSMEDCON 2015, Kolkata. Asian Journal of Transfusion Science. 2016; 10:1.