Review Article

Promoting Cardiovascular Health: How Blood Transfusions Contribute to HIV Patient Well-being

Emmanuel Ifeanyi Obeagu*

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

*Corresponding Author: Emmanuel Ifeanyi Obeagu, Department of Medical Laboratory Science, Kampala International University, Uganda.

Received Date: July 15, 2024 | Accepted Date: August 02, 2024 | Published Date: August 19, 2024

Citation: Emmanuel I. Obeagu, (2024), Promoting Cardiovascular Health: How Blood Transfusions Contribute to HIV Patient Well-being, *Journal of Clinical and Laboratory Research*, 7(7); **DOI:**10.31579/2768-0487/145

Copyright: © 2024, Emmanuel Ifeanyi Obeagu. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

Abstract

Blood transfusions are a critical therapeutic intervention for individuals living with HIV, primarily for managing anemia and enhancing overall health outcomes. Recent evidence suggests that blood transfusions may also play a significant role in promoting cardiovascular health in this population. This review explores the mechanisms through which blood transfusions positively impact cardiovascular well-being, including the restoration of hemoglobin levels, improved oxygen delivery to tissues, and modulation of immune function and inflammation. Anemia is prevalent among HIV patients and contributes to fatigue and weakness, which can exacerbate cardiovascular risk factors. By effectively increasing hemoglobin levels and improving blood circulation, transfusions can alleviate these symptoms, thereby enhancing patients' energy levels and capacity for physical activity. Improved cardiovascular health is essential for mitigating long-term complications associated with HIV, as individuals living with the virus are at a higher risk for cardiovascular disease. By integrating blood transfusions into comprehensive care plans, healthcare providers can enhance the overall well-being and quality of life for individuals living with HIV.

Key words: blood transfusions; cardiovascular health; HIV; well-being; anemia

Introduction

The advent of antiretroviral therapy (ART) has significantly improved the prognosis for individuals living with HIV, transforming what was once a fatal diagnosis into a manageable chronic condition. As a result, the focus of HIV care has shifted from merely controlling viral replication to addressing comorbidities and improving the overall quality of life for patients. Among the prevalent issues faced by individuals with HIV, anemia and cardiovascular disease (CVD) are two critical concerns that can greatly affect health outcomes. The complex interplay between these conditions necessitates a comprehensive approach to patient management. [1-2] Anemia is a common complication in individuals living with HIV, with prevalence rates reported between 30% and 50%. This condition can arise from various factors, including the effects of HIV on bone marrow function, opportunistic infections, nutritional deficiencies, and the side effects of certain antiretroviral medications. The resulting decrease in hemoglobin levels can lead to debilitating symptoms such as fatigue, weakness, and decreased exercise tolerance. These symptoms can severely impair the quality of life and contribute to further health complications, including cardiovascular issues. [3-5] Cardiovascular disease has emerged as a significant cause of morbidity and mortality among individuals with HIV. Research indicates that patients living with HIV are at an increased risk for developing CVD compared to the general population. Factors contributing

Auctores Publishing LLC – Volume 7(7)-145 www.auctoresonline.org ISSN: 2768-0487 to this elevated risk include chronic inflammation, immune activation, and metabolic abnormalities associated with HIV infection and ART. Consequently, addressing cardiovascular health is paramount in the management of individuals living with HIV, particularly as they age and accumulate additional risk factors. [6-7] Blood transfusions have been a longstanding intervention for managing anemia in various patient populations, including those with HIV. By effectively restoring hemoglobin levels, blood transfusions improve oxygen delivery to tissues, enhancing overall health and well-being. Beyond their role in correcting anemia, emerging evidence suggests that blood transfusions may also confer additional benefits for cardiovascular health. This multifaceted impact warrants further exploration to understand how transfusions can be integrated into comprehensive HIV care strategies.8

Several mechanisms underlie the potential cardiovascular benefits of blood transfusions. Improved oxygenation resulting from transfusion therapy is crucial for maintaining optimal myocardial metabolism and function. Additionally, transfusions may enhance immune function and modulate inflammatory responses, which are vital for preventing cardiovascular complications. By alleviating fatigue and weakness associated with anemia, transfusions can also enable patients to engage in physical activities, further supporting cardiovascular fitness. [9-10] Despite the benefits, the use of

blood transfusions in HIV care raises important considerations. Potential risks associated with transfusion therapy, such as transfusion reactions and infection transmission, must be carefully weighed against the potential advantages. Therefore, individualized transfusion protocols and monitoring strategies are essential to ensure patient safety and optimize outcomes. [11]

Mechanisms of Action

Blood transfusions primarily function to restore hemoglobin levels, thereby enhancing oxygen delivery to tissues and promoting overall well-being. However, their impact extends beyond simple restoration of oxygen transport. One of the primary benefits of blood transfusions is the rapid increase in hemoglobin levels. Hemoglobin, the oxygen-carrying component of red blood cells, is critical for delivering oxygen to tissues throughout the body. In individuals with anemia, low hemoglobin levels result in reduced oxygen availability, leading to fatigue and decreased physical performance. Blood transfusions effectively restore hemoglobin levels, enhancing oxygen transport and alleviating symptoms associated with anemia, which is crucial for maintaining optimal cardiovascular function. [12-13] Beyond simply increasing hemoglobin levels, blood transfusions improve overall blood volume and enhance circulation, leading to more efficient oxygen delivery to tissues, including the heart and muscles. This improved perfusion is vital for maintaining cardiovascular health, as adequate oxygenation is necessary for preventing ischemia and supporting cellular metabolism in the heart. Enhanced oxygen delivery helps ensure that the myocardium receives sufficient oxygen to meet its metabolic demands, reducing the risk of cardiovascular complications. [13-14] Blood transfusions may also positively affect immune function, particularly in individuals living with HIV. By enhancing the oxygen supply to immune cells, transfusions can improve their activity and proliferation, bolstering the body's ability to combat infections and inflammation. A robust immune response is critical for preventing opportunistic infections that can exacerbate anemia and cardiovascular risk factors. Improved immune function can contribute to better overall health and mitigate complications related to both HIV and cardiovascular disease. [15-16]

Chronic inflammation is a hallmark of HIV infection and a significant contributor to cardiovascular disease. Blood transfusions can help modulate inflammatory responses by improving oxygenation and reducing the production of pro-inflammatory cytokines. Enhanced oxygen delivery to tissues may decrease hypoxia-induced inflammation, thereby reducing vascular inflammation and promoting vascular health. By mitigating inflammatory processes, blood transfusions can potentially lower the risk of cardiovascular complications associated with HIV. [16-17] The fatigue and weakness associated with anemia can significantly impact the quality of life for individuals living with HIV. Blood transfusions effectively alleviate these symptoms by restoring hemoglobin levels and improving energy levels. Increased energy enables patients to engage in physical activities, which are essential for cardiovascular fitness. Regular physical activity is associated with improved cardiovascular health outcomes, making the improvement of energy levels through transfusions a critical component of holistic HIV care. [17-18] In individuals with HIV, anemia can contribute to myocardial ischemia due to inadequate oxygen delivery to the heart muscle. By increasing hemoglobin levels and enhancing oxygenation, blood transfusions can help prevent ischemic events, thereby supporting heart health. This is particularly important in patients with existing cardiovascular risk factors, as timely transfusions can mitigate the adverse effects of anemia on cardiac function. [19-20]

Copy rights @ Emmanuel Ifeanyi Obeagu.

Chronic anemia may lead to maladaptive cardiovascular remodeling, characterized by alterations in heart structure and function. Blood transfusions can counteract these effects by restoring normal hemoglobin levels and improving overall hemodynamics. By promoting adequate oxygen delivery to the myocardium, transfusions may support healthier heart remodeling and function, reducing the long-term risks associated with heart disease in HIV patients. [21-22] The restoration of hemoglobin levels through transfusion therapy enhances exercise capacity in individuals living with HIV. Improved exercise tolerance not only contributes to better cardiovascular health but also supports mental well-being by allowing patients to engage in physical activities that promote overall health. Regular physical activity is associated with a reduced risk of cardiovascular disease. making enhanced exercise capacity an important goal in HIV management. [23-24] Blood transfusions may indirectly help reduce cardiovascular risk factors in individuals living with HIV. By improving anemia-related symptoms and enhancing overall health, transfusions can lead to better adherence to treatment regimens, increased engagement in healthy lifestyle behaviors, and improved management of comorbid conditions such as hypertension and diabetes. Addressing these risk factors is crucial for promoting long-term cardiovascular health in HIV patients. [25-26]

Clinical Evidence

The clinical evidence supporting the role of blood transfusions in promoting cardiovascular health among individuals living with HIV is increasingly recognized. Several studies have demonstrated the benefits of transfusion therapy, particularly in alleviating anemia and its associated symptoms. Numerous studies have shown that blood transfusions effectively restore hemoglobin levels in HIV patients suffering from anemia. These improvements are crucial, as enhanced hemoglobin levels facilitate better oxygen delivery to tissues, supporting cardiovascular function and reducing the risk of complications. [27-28] Research indicates that blood transfusions can lead to improved exercise capacity in individuals living with HIV. Improved exercise capacity is particularly important for cardiovascular health, as regular physical activity is associated with reduced cardiovascular risk and enhanced overall well-being. Blood transfusions may also contribute to enhanced immune function and reduced inflammation, both of which are vital for cardiovascular health in HIV patients. Additionally, transfusions have been linked to reductions in inflammatory markers, suggesting a potential role in mitigating the chronic inflammation that characterizes HIV infection and contributes to cardiovascular risk. [29-31] Longitudinal studies examining the long-term effects of blood transfusions on cardiovascular morbidity in HIV patients provide valuable insights. These findings suggest that transfusions may play a protective role in preventing cardiovascular complications in individuals living with HIV. The relationship between blood transfusions and the prevention of myocardial ischemia in HIV patients has also been explored. This effect is particularly important for patients with anemia, as they are at higher risk for ischemia due to impaired oxygen transport. [32-33]

Improvements in quality-of-life following blood transfusions have been well-documented in HIV patients. These subjective improvements are vital for patient engagement and adherence to treatment regimens, contributing to better overall health outcomes. Long-term studies evaluating the effects of blood transfusions on health outcomes in HIV patients are essential for understanding their overall benefits. These findings underscore the potential for transfusions to not only address immediate hematological concerns but also to enhance long-term health outcomes and cardiovascular well-being. [34-35] While the benefits of blood transfusions in HIV patients are well-

documented, it is essential to conduct thorough risk-benefit analyses. Studies have indicated that the advantages of improved hemoglobin levels and cardiovascular health often outweigh the potential risks, such as transfusion reactions or the transmission of infectious agents. Healthcare providers must carefully evaluate each patient's unique circumstances to determine the appropriateness of transfusion therapy. [36]

Implications for Transfusion Strategies

The positive impact of blood transfusions on cardiovascular health among individuals living with HIV underscores the need for well-defined transfusion strategies tailored to this unique patient population. Implementing effective transfusion protocols can maximize the benefits of transfusion therapy while minimizing associated risks. Transfusion strategies should be individualized based on each patient's clinical condition, hemoglobin levels, symptoms, and overall health status. A comprehensive assessment of anemia severity and its impact on quality of life can guide transfusion decisions. Tailoring transfusion protocols allows healthcare providers to address specific patient needs and optimize outcomes, ensuring that transfusions are performed when the potential benefits outweigh the risks. [37-39] Regular monitoring of hemoglobin levels is crucial for identifying patients who may benefit from transfusions. Establishing a routine schedule for hemoglobin assessments can help healthcare providers detect anemia early and initiate transfusion therapy when necessary. By maintaining close monitoring, clinicians can avoid unnecessary transfusions while ensuring timely intervention for patients with significant anemiarelated symptoms. [40] Integrating a multidisciplinary care approach that includes hematologists, infectious disease specialists, and nutritionists can enhance transfusion strategies. Collaboration among healthcare providers enables a holistic assessment of patients' needs, including addressing nutritional deficiencies, optimizing antiretroviral therapy, and managing comorbid conditions. This team-based approach fosters comprehensive care that prioritizes both hematological and cardiovascular health. [41]

Empowering patients through education about the benefits and risks of blood transfusions is essential for informed decision-making. Providing patients with clear information about how transfusions can improve their symptoms, enhance energy levels, and promote cardiovascular health encourages active participation in their care. Engaging patients in discussions about transfusion options fosters adherence to treatment plans and enhances patient satisfaction. [42] Conducting thorough risk assessments prior to blood transfusions is critical for ensuring patient safety. Healthcare providers should evaluate potential risks, such as transfusion reactions and infection transmission, and implement strategies to mitigate these risks. For instance, using leukocyte-reduced blood products can help reduce the risk of febrile non-hemolytic reactions. Clear protocols for monitoring patients during and after transfusions are also necessary to identify and manage any adverse reactions promptly. [43] Long-term follow-up is essential for evaluating the effects of blood transfusions on both hematological and cardiovascular health. Healthcare providers should establish follow-up protocols to assess the sustainability of hemoglobin improvements and monitor cardiovascular risk factors. Regular evaluations can help identify any emerging complications and guide ongoing management strategies, ensuring that patients continue to benefit from transfusion therapy. [40] Incorporating blood transfusions into comprehensive care models for HIV patients is crucial for promoting overall health and well-being. Transfusion therapy should be viewed as one component of a holistic approach that addresses all aspects of patients' health, including nutritional support, mental health services, and lifestyle modifications. A comprehensive care model can facilitate better patient engagement and improve overall health outcomes. [42] Implementing continuous quality improvement initiatives within transfusion services can enhance the safety and effectiveness of blood transfusions in HIV care. Regularly reviewing transfusion practices, assessing patient outcomes, and soliciting feedback from healthcare providers can identify areas for improvement. This commitment to quality can ensure that transfusion strategies remain effective and responsive to the needs of individuals living with HIV. [43]

Conclusion

Blood transfusions serve as a vital therapeutic intervention for individuals living with HIV, offering significant benefits that extend beyond the management of anemia. The evidence presented in this review underscores the positive impact of transfusions on cardiovascular health, highlighting their role in restoring hemoglobin levels, improving oxygen delivery, and enhancing overall quality of life. By alleviating symptoms associated with anemia and promoting better cardiovascular outcomes, blood transfusions play a crucial role in comprehensive HIV care.

The mechanisms by which blood transfusions contribute to cardiovascular well-being include enhanced immune function, reduced inflammation, and improved exercise capacity. These factors are particularly important given the increased risk of cardiovascular disease among individuals living with HIV. The findings suggest that integrating blood transfusions into tailored care strategies can lead to improved patient outcomes, decreased morbidity, and enhanced quality of life.

References

- Obeagu EI, Obeagu, GU. (2024). Counting Cells, Shaping Fates: CD4/CD8 Ratios in HIV. *Elite Journal of Scientific Research and Review*; 2(1): 37-50
- Obeagu EI, Obeagu GU. (2024). Hematological Changes Following Blood Transfusion in Young Children with Severe Malaria and HIV: A Critical Review. *Elite Journal of Laboratory Medicine*; 2(1): 33-45
- Obeagu EI, Obeagu GU. (2024). The Role of Blood Transfusion Strategies in HIV Management: Current Insights and Future Directions. *Elite Journal of Medicine*; 2(1):10-22
- 4. Obeagu EI, Obeagu GU, Ukibe NR, Oyebadejo SA. (2024). Anemia, iron, and HIV: decoding the interconnected pathways: A review. *Medicine*;103(2): e36937.
- Volberding P. (2002). The impact of anemia on quality of life in human immunodeficiency virus—infected patients. *The Journal* of infectious diseases ;185(Supplement_2): S110-114.
- Montoro M, Cucala M, Lanas Á, Villanueva C, Hervás AJ, et al. (2022). Indications and hemoglobin thresholds for red blood cell transfusion and iron replacement in adults with gastrointestinal bleeding: An algorithm proposed by gastroenterologists and patient blood management experts. *Frontiers in Medicine*; 9:903739.
- Obeagu EI, Obeagu GU. (2024). Eosinophil Dynamics in Pregnancy among Women Living with HIV: A Comprehensive Review. *Int. J. Curr. Res. Med. Sci*;10(1):11-24.
- Viola N, Kimono E, Nuruh N, Obeagu EI. (2023). 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.;3(2):7-14.

- 9. Busch MP, Bloch EM, Kleinman S. (2019). Prevention of transfusion-transmitted infections. Blood, *The Journal of the American Society of Hematology*;133(17):1854-1864.
- Obeagu EI, Obeagu GU. (2024). Transfusion-Related Complications in Children Under 5 with Coexisting HIV and Severe Malaria: A Review. Int. J. Curr. Res. Chem. Pharm. Sci.;11(2):9-19.
- 11. 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).
- 12. Heron SE, Elahi S. (2017). HIV infection and compromised mucosal immunity: oral manifestations and systemic inflammation. *Frontiers in immunology*; 8:241.
- 13. Obeagu EI, Obeagu, GU. (2024). P-Selectin and Platelet Activation in HIV: Implications for Antiviral Therapy. *Elite Journal of Scientific Research and Review*; 2(1): 17-41
- 14. Obeagu EI, Obeagu GU. (2024). The Intricate Relationship Between Erythropoietin and HIV-Induced Anemia: Unraveling Pathways for Therapeutic Insights. *Int. J. Curr. Res. Chem. Pharm. Sci*;11(2):30-40.
- Obeagu EI, Anyiam AF, Obeagu GU. (2024). Erythropoietin Therapy in HIV-Infected Individuals: A Critical Review. *Elite Journal of HIV*; 2(1): 51-64
- Obeagu EI, Obeagu GU. (2024). Strength in Unity: Building Support Networks for HIV Patients in Uganda. *Elite Journal of Medicine*; 2(1): 1-16
- 17. Bloch EM, Vermeulen M, Murphy E. (2012). Blood transfusion safety in Africa: a literature review of infectious disease and organizational challenges. *Transfusion medicine reviews.*;26(2):164-180.
- Obeagu EI, Obeagu GU. (2024). Eosinophilic Changes in Placental Tissues of HIV-Positive Pregnant Women: A Review. *Elite Journal of Laboratory Medicine*; 2(1): 14-32
- Obeagu EI, Obeagu, GU. (2024). The Crucial Role of Erythropoietin in Managing Anemia in HIV: A Review. *Elite Journal of Scientific Research and Review*; 2(1): 24-36
- Cunningham-Rundles S, McNeeley DF, Moon A. (2005). Mechanisms of nutrient modulation of the immune response. *Journal of Allergy and Clinical immunology*;115(6):1119-1128.
- Obeagu EI, Ubosi NI, Obeagu GU, Obeagu AA. (2024). Nutritional Strategies for Enhancing Immune Resilience in HIV: A Review. Int. J. Curr. Res. Chem. Pharm. Sci.;11(2):41-51.
- Obeagu EI, Obeagu GU. (2024). Assessing Platelet Functionality in HIV Patients Receiving Antiretroviral Therapy: Implications for Risk Assessment. *Elite Journal of HIV*; 2(3): 14-26
- Obeagu EI, Elamin EAI Obeagu GU. (2024). Understanding the Intersection of Highly Active Antiretroviral Therapy and Platelets in HIV Patients: A Review. *Elite Journal of Haematology*; 2(3): 111-117
- 24. Lotfi R, Kaltenmeier C, Lotze MT, Bergmann C. (2016). Until death do us part: necrosis and oxidation promote the tumor microenvironment. *Transfusion Medicine and Hemotherapy*;43(2):120-32.
- Cunha PP, Minogue E, Krause LC, Hess RM, Bargiela D, et al. (2023). Oxygen levels at the time of activation determine T cell persistence and immunotherapeutic efficacy. *Elife*.;12: e84280.

- Obeagu EI, Obeagu GU. (2024). Neonatal Outcomes in Children Born to Mothers with Severe Malaria, HIV, and Transfusion History: A Review. *Elite Journal of Nursing and Health Science*; 2(3): 38-58
- Obeagu EI. (2024). Erythropoietin and the Immune System: Relevance in HIV Management. *Elite Journal of Health Science*; 2(3): 23-35
- Zicari S, Sessa L, Cotugno N, Ruggiero A, Morrocchi E, et al. (2019). Immune activation, inflammation, and non-AIDS comorbidities in HIV-infected patients under long-term ART. *Viruses* ;11(3):200.
- 29. Obeagu EI, Obeagu GU. (2024). Understanding Immune Cell Trafficking in Tuberculosis-HIV Coinfection: The Role of Lselectin Pathways. *Elite Journal of Immunology*; 2(2): 43-59
- Obeagu EI, Obeagu GU. (2024). Anemia and Erythropoietin: Key Players in HIV Disease Progression. *Elite Journal of Haematology*; 2(3): 42-57
- Balderson BH, Grothaus L, Harrison RG, McCoy K, Mahoney C, et al. (2013). Chronic illness burden and quality of life in an aging HIV population. *AIDS care*;25(4):451-458.
- 32. Obeagu EI, Ayogu EE, Obeagu GU. (2024). Impact on Viral Load Dynamics: Understanding the Interplay between Blood Transfusion and Antiretroviral Therapy in HIV Management. *Elite Journal of Nursing and Health Science*; 2(2): 5-15
- Obeagu EI, Obeagu GU. (2024). Immune Modulation in HIV-Positive Neonates: Insights and Implications for Clinical Management. *Elite Journal of Nursing and Health Science*; 2(3): 59-72
- 34. Chakraborty R, Cannella L, Cottone F, Efficace F. (2020). Quality of patient-reported outcome reporting in randomised controlled trials of haematological malignancies according to international quality standards: a systematic review. *The Lancet Haematology*;7(12): e892-901.
- Hébert PC, Fergusson D, Blajchman MA, Wells GA, Kmetic A, et al. (2003). Clinical outcomes following institution of the Canadian universal leukoreduction program for red blood cell transfusions. *Jama*; 289(15):1941-1949.
- 36. Vamvakas EC, Blajchman MA. (2009). Transfusion-related mortality: the ongoing risks of allogeneic blood transfusion and the available strategies for their prevention. Blood, *The Journal of the American Society of Hematology*;113(15):3406-3417.
- 37. Kaur P, Basu S. (2005). Transfusion-transmitted infections: existing and emerging pathogens. *Journal of postgraduate medicine*.;51(2):146-151.
- Wiersum-Osselton JC, Whitaker B, Grey S, Land K, Perez G, et al. (2019). Revised international surveillance case definition of transfusion-associated circulatory overload: a classification agreement validation study. *The Lancet Haematology*;6(7): e350-358.
- 39. Smit-Sibinga C, Pitman JP. Transmission of HIV through blood—how to bridge the knowledge gap. InHIV and AIDS-Updates on biology, immunology, epidemiology and treatment strategies 2011: 583-618. InTech, Rijeka, Croatia.
- Slonim AD, Bish EK, Xie RS. (2014). Red blood cell transfusion safety: probabilistic risk assessment and cost/benefits of risk reduction strategies. *Annals of Operations Research*; 221:377-406.

Copy rights @ Emmanuel Ifeanyi Obeagu.

- Steffen KM, Spinella PC, Holdsworth LM, Ford MA, Lee GM, et al. (2021). Factors influencing implementation of blood transfusion recommendations in pediatric critical care units. *Frontiers in Pediatrics*; 9:800461.
- 42. Barro L, Drew VJ, Poda GG, Tagny CT, El-Ekiaby M, et al. (2018). Blood transfusion in sub-Saharan Africa: understanding

the missing gap and responding to present and future challenges. *Vox Sanguinis*;113(8):726-736.

43. Ako S, Njunda LA, Akum EA, Benjamin PT, Assob J. (2018). Hematological related disorders and transfusion of HIV patients on highly active antiretroviral therapy (HAART) in the South West Region of Cameroon: hematological monitory parameters for HIV follow-up. J HIV Retrovirus;4(1):5.



This work is licensed under Creative Commons Attribution 4.0 License

Submit Manuscript

To Submit Your Article, Click Here:

DOI:10.31579/2768-0487/145

- Ready to submit your research? Choose Auctores and benefit from:
 - fast, convenient online submission
 - > rigorous peer review by experienced research in your field
 - rapid publication on acceptance
 - > authors retain copyrights
 - > unique DOI for all articles
 - immediate, unrestricted online access

At Auctores, research is always in progress.

Learn more https://auctoresonline.org/journals/journal-of-clinical-and-laboratory-research