Sickle Cell Anemia and Pregnancy Hemolysis: Clinical Considerations

Article *in* Middle East Research Journal of Nursing · October 2024

DOI: 10.36348/merjn.2024.v04i05.003

2 authors:

Emmanuel Ifeanyi Obeagu
Africa University
2,100 PUBLICATIONS **36,090** CITATIONS
SEE PROFILE

Getrude Uzoma Obeagu
Kampala International University
649 PUBLICATIONS **18,724** CITATIONS
SEE PROFILE

Middle East Research Journal of Nursing
ISSN 2789-8679 (Print) & ISSN: 2958-2016 (Online)
Frequency: Bi-Monthly
DOI: https://doi.org/10.36348/merjn.2024.v04i05.003

KUWAIT SCHOLARS PUBLISHER
Website: http://www.kspublisher.com/
Email: office@kspublisher.com

Sickle Cell Anemia and Pregnancy Hemolysis: Clinical Considerations

Emmanuel Ifeanyi Obeagu[1*], Getrude Uzoma Obeagu[2]
[1]Department of Medical Laboratory Science, Kampala International University, Ishaka, Uganda
[2]School of Nursing Science, Kampala International University, Ishaka, Uganda

Abstract: Sickle cell anemia (SCA) is a hereditary blood disorder characterized by abnormal hemoglobin production, leading to chronic hemolysis and episodic vaso-occlusive crises (VOCs). Pregnancy in women with SCA poses significant clinical challenges due to the increased physiological demands, which exacerbate hemolysis and increase maternal and fetal risks. This review explores the pathophysiology of hemolysis in SCA during pregnancy, its clinical implications, and management strategies aimed at improving maternal and fetal outcomes. Hemolysis can result in severe anemia, acute chest syndrome, increased risk of infections, and adverse fetal outcomes, such as intrauterine growth restriction and preterm delivery. Management strategies for hemolysis in pregnancy include blood transfusions, pharmacological therapies, nutritional supplementation, and emerging treatments like gene therapy. Blood transfusions are widely used to mitigate anemia and reduce the number of circulating sickled cells, while pharmacological agents such as L-glutamine help address oxidative stress. Nutritional support, particularly with folic acid and antioxidants, is essential in promoting healthy red blood cell production and mitigating oxidative damage. Emerging therapies like gene editing offer promising future directions for more effective management of SCA and pregnancy-related hemolysis.

Keywords: Sickle Cell Anemia, Hemolysis, Pregnancy, Maternal Complications, Fetal Outcomes.

Review Paper

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

How to cite this paper:
Emmanuel Ifeanyi Obeagu & Getrude Uzoma Obeagu (2024). Sickle Cell Anemia and Pregnancy Hemolysis: Clinical Considerations. *Middle East Res J Nursing*, *4*(5): 72-75.

Article History:
| Submit: 23.09.2024 |
| Accepted: 24.10.2024 |
| Published: 26.10.2024 |

INTRODUCTION

Sickle cell anemia (SCA) is a hereditary hemoglobinopathy caused by a mutation in the β-globin gene, leading to the production of abnormal hemoglobin S (HbS). Under conditions of low oxygen tension, HbS polymerizes, causing red blood cells (RBCs) to become rigid, sickle-shaped, and prone to destruction. This characteristic sickling leads to chronic hemolysis, vaso-occlusive crises (VOCs), and multi-system complications. SCA predominantly affects individuals of African, Mediterranean, Middle Eastern, and Indian ancestry, with significant prevalence in sub-Saharan Africa and among populations of African descent globally. Hemolysis, a key pathological feature of SCA, presents a unique set of challenges during pregnancy, a period characterized by increased oxygen and nutrient demands [1-4]. Pregnancy in women with SCA is considered high-risk due to the physiological changes that exacerbate the underlying complications of the disease, particularly hemolysis and anemia. During pregnancy, maternal blood volume increases by up to 50%, and the cardiovascular system undergoes significant adaptations to meet the growing oxygen and metabolic demands of the fetus. However, in women with SCA, the increased demands often overwhelm the already compromised oxygen-carrying capacity of the sickled RBCs. This leads to accelerated hemolysis, further depleting hemoglobin levels and heightening the risk of severe maternal and fetal complications [5-7].

Hemolysis during pregnancy in women with SCA not only contributes to worsening anemia but also exacerbates systemic inflammation, endothelial dysfunction, and oxidative stress. These processes can lead to severe maternal complications such as acute chest syndrome, thromboembolic events, and infections, which are major causes of maternal morbidity and mortality in this population. Additionally, the chronic hemolytic state increases the risk of obstetric complications, including preeclampsia, preterm labor, intrauterine growth restriction (IUGR), and stillbirth. The delicate balance between managing SCA-related hemolysis and ensuring favorable pregnancy outcomes requires a tailored and multidisciplinary approach to care [8-11]. From a fetal perspective, maternal hemolysis during pregnancy can significantly impact placental function, leading to inadequate oxygen and nutrient delivery. This can result in adverse outcomes such as IUGR, low birth weight, and preterm delivery.

Furthermore, sickling of RBCs within the placental vasculature can cause placental infarctions and reduced placental perfusion, which directly compromises fetal growth and development. Hence, managing hemolysis in SCA pregnancies not only focuses on maternal well-being but also on safeguarding fetal health through timely and appropriate interventions [12, 13]. Management of hemolysis in pregnant women with SCA involves several strategies aimed at reducing the rate of RBC destruction, optimizing oxygen delivery, and preventing complications. Blood transfusions are one of the most effective interventions for managing severe anemia and reducing the proportion of sickled RBCs in circulation. However, transfusion therapy is not without risks, including iron overload, alloimmunization, and increased susceptibility to infections. Other therapeutic approaches include pharmacological interventions like L-glutamine to reduce oxidative stress, hydration to improve blood flow, and folic acid supplementation to support erythropoiesis. Newer therapies, such as gene editing and hydroxyurea alternatives, hold promise for reducing hemolysis in the long term, though their safety during pregnancy remains under investigation [14-16].

Pathophysiology of Hemolysis in Sickle Cell Anemia

Hemolysis in sickle cell anemia (SCA) is driven by the abnormal properties of hemoglobin S (HbS), which leads to the characteristic deformation of red blood cells (RBCs) and their premature destruction. Under conditions of low oxygen tension, HbS polymerizes, causing RBCs to adopt a rigid, crescent or sickle shape. This structural change reduces the flexibility of RBCs, making it difficult for them to pass through the microvasculature. Sickled cells are prone to hemolysis due to mechanical stress and the intrinsic instability of the membrane, leading to chronic hemolytic anemia [17, 18]. There are two main types of hemolysis in SCA: intravascular and extravascular. Intravascular hemolysis occurs when sickled RBCs rupture within the bloodstream, releasing free hemoglobin, which depletes nitric oxide (NO) and contributes to vasculopathy. Nitric oxide is critical for vascular relaxation and smooth muscle function, so its depletion results in vasoconstriction and endothelial dysfunction, exacerbating the clinical manifestations of SCA, such as vaso-occlusive crises (VOCs). Extravascular hemolysis, on the other hand, occurs when sickled RBCs are sequestered and destroyed by macrophages in the spleen and liver. This process further reduces RBC lifespan and contributes to the chronic anemia seen in SCA [19, 20].

The continuous cycle of hemolysis in SCA triggers a cascade of pathological events that extend beyond the destruction of RBCs. Hemolysis releases free heme and iron, which are potent sources of oxidative stress, further damaging the RBC membrane and promoting more hemolysis. The chronic hemolytic state leads to systemic inflammation, endothelial injury, and activation of the coagulation cascade, increasing the risk of thrombotic events. Additionally, the destruction of RBCs depletes critical factors such as haptoglobin and hemopexin, which normally bind free hemoglobin and heme, respectively, to mitigate their harmful effects. This depletion further amplifies oxidative stress and inflammation, contributing to the multi-organ complications seen in SCA, including acute chest syndrome, pulmonary hypertension, and renal impairment [21, 22]. In pregnancy, the pathophysiological consequences of hemolysis are magnified due to the increased oxygen demand and cardiovascular adaptations that occur to support fetal development. The combination of maternal hemolysis and the physiological stress of pregnancy poses significant risks to both maternal and fetal health [23].

Clinical Implications of Hemolysis in Pregnancy

Hemolysis during pregnancy in women with SCA significantly impacts maternal and fetal health. Maternal complications include an increased risk of acute chest syndrome, infections, VOCs, and worsening anemia. Acute chest syndrome, a form of acute lung injury, is a leading cause of maternal morbidity and mortality in SCA. The combination of hemolysis, inflammation, and infection during pregnancy increases the risk of this life-threatening condition. Moreover, the chronic anemia resulting from hemolysis can lead to fatigue, reduced exercise tolerance, and cardiovascular strain [24]. Fetal complications are also a major concern in pregnancies complicated by SCA. Hemolysis and anemia impair placental function, leading to inadequate oxygen and nutrient delivery to the fetus. This increases the risk of intrauterine growth restriction, preterm delivery, and low birth weight. Additionally, maternal hemolytic crises and VOCs can lead to placental insufficiency, which can cause fetal distress and the need for early delivery. The combination of maternal and fetal risks underscores the importance of proactive management and close monitoring throughout pregnancy. The interplay between hemolysis and pregnancy creates a delicate balance, as both maternal and fetal health can be compromised by the underlying pathophysiological processes of SCA. Hemolysis not only worsens anemia but also contributes to systemic inflammation and vascular damage, which can lead to a range of complications.

Management Strategies for Hemolysis in Pregnancy

Managing hemolysis in pregnant women with SCA requires a multidisciplinary approach and tailored interventions to minimize the risks to both the mother and fetus. Blood transfusion therapy is a mainstay of treatment, helping to increase hemoglobin levels and reduce the proportion of sickled RBCs in circulation. Regular transfusions, particularly exchange transfusions, can reduce the frequency of VOCs and improve oxygenation, thereby mitigating the effects of hemolysis. However, transfusion therapy must be carefully managed to avoid complications such as iron overload and

alloimmunization [21]. Pharmacological interventions play a key role in managing hemolysis and its complications during pregnancy. Hydroxyurea, a drug commonly used to increase fetal hemoglobin (HbF) levels, is generally avoided during pregnancy due to concerns about teratogenic effects. However, its use in select patients is being reconsidered. Other agents, such as L-glutamine, which reduces oxidative stress, and anticoagulants to prevent thromboembolic events, may be employed in managing the inflammatory and vascular complications associated with hemolysis. Antioxidant therapy and hydration are also important components of supportive care to reduce oxidative stress and improve blood flow [22]. Nutritional support is essential for managing anemia and hemolysis in pregnancy. Pregnant women with SCA require increased amounts of folic acid to support RBC production and prevent folate deficiency anemia. Adequate hydration and a diet rich in antioxidants are also crucial in reducing oxidative damage and maintaining healthy RBC function. The use of iron chelation therapy may be necessary for patients receiving frequent blood transfusions to prevent iron overload [23].

Emerging Therapies and Future Directions

Emerging therapies offer hope for the future management of hemolysis in pregnant women with SCA. Gene therapy, including CRISPR-Cas9 techniques, aims to correct the genetic mutation responsible for SCA, potentially providing a curative option. Although gene therapy is still in its experimental stages, it has shown promise in reducing hemolysis and improving overall disease outcomes. L-glutamine therapy, which reduces oxidative stress, has been approved for use in SCA patients and represents a potential option for managing hemolysis during pregnancy, although more studies are needed to assess its safety in pregnant women. Other promising treatments include P-selectin inhibitors, which target the adhesion of sickled RBCs to the endothelium, reducing the risk of VOCs and hemolysis. These emerging therapies may offer new ways to manage the complications of hemolysis and improve maternal and fetal outcomes in pregnancies complicated by SCA. Continued research into these therapies is essential for advancing the care of pregnant women with SCA and developing safer and more effective treatment options [24].

CONCLUSION

Hemolysis in pregnant women with sickle cell anemia presents significant clinical challenges that require a comprehensive and multidisciplinary approach to care. The pathophysiology of hemolysis, characterized by both intravascular and extravascular destruction of RBCs, leads to chronic anemia, inflammation, and vascular complications, all of which are exacerbated during pregnancy. Managing hemolysis effectively is critical to improving both maternal and fetal outcomes. Blood transfusion therapy, pharmacological interventions, nutritional support, and emerging therapies all play important roles in managing hemolysis and its associated complications. Close monitoring of maternal and fetal health is essential to detect and manage complications early. With ongoing research into new treatments, there is hope for improved outcomes and safer pregnancies for women with SCA.

REFERENCES

1. Obeagu, E. I., Ochei, K. C., Nwachukwu, B. N., & Nchuma, B. O. (2015). Sickle cell anaemia: a review. *Scholars Journal of Applied Medical Sciences*, *3*(6B), 2244-52.
2. Obeagu, E. I. (2020). Erythropoeitin in sickle cell anaemia: a review. *International Journal of Research Studies in Medical and Health Sciences*, *5*(2), 22-8.
3. Obeagu, E. I., & Agreen, F. C. (2023). Anaemia among pregnant women: A review of African pregnant teenagers. *J Pub Health Nutri. 2023; 6 (1), 138*.
4. Obeagu, E. I., Obeagu, G. U., Chukwueze, C. M., Ikpenwa, J. N., & Ramos, G. F. (2022). 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*, *2*(2), 1-9.
5. Obeagu, E. I., Obeagu, G. U., & Hauwa, B. A. Optimizing Maternal Health: Addressing Hemolysis in Pregnant Women with Sickle Cell Anemia. *Journal home page*: http://www. journalijiar.com.12(01).
6. Helvaci, M. R., Yilmaz, H., Yalcin, A., Muftuoglu, O. E., Abyad, A., & Pocock, L. (2021). Sickle cell anemia versus sickle cell diseases in adults. *Middle East Journal of Internal Medicine*, *14*(2).
7. van't Oever, R. M., Zwiers, C., de Winter, D., de Haas, M., Oepkes, D., Lopriore, E., & Verweij, E. J. (2022). Identification and management of fetal anemia due to hemolytic disease. *Expert Review of Hematology*, *15*(11), 987-998.
8. Feinberg, A. N., Shwayder, T. A., Tareen, R. S., & Tempark, T. (2013). Perspectives on management of pediatric dermatologic disorders. *Pediatric Psychodermatology: A Clinical Manual of Child and Adolescent Psychoneurocutaneous Disorders*, 3-68.
9. Muñoz, M., Peña-Rosas, J. P., Robinson, S., Milman, N., Holzgreve, W., Breymann, C., ... & Hardy, J. F. (2018). Patient blood management in obstetrics: management of anaemia and haematinic deficiencies in pregnancy and in the post-partum period: NATA consensus statement. *Transfusion medicine*, *28*(1), 22-39.
10. Obeagu, E. I., & Obeagu, G. U. (2024). Implications of climatic change on sickle cell anemia: A review. *Medicine*, *103*(6), e37127.

11. Obeagu, E. I. (2023). Depression in sickle cell anemia: an overlooked battle. *Int. J. Curr. Res. Chem. Pharm. Sci*, *10*(10), 41-4.
12. Obeagu, E. I., Ubosi, N. I., Obeagu, G. U., Egba, S. I., & Bluth, M. H. (2024). Understanding apoptosis in sickle cell anemia patients: Mechanisms and implications. *Medicine*, *103*(2), e36898.
13. Obeagu, E. I., & Obeagu, G. U. (2024). Oxidative Damage and Vascular Complications in Sickle Cell Anemia: A Review. *Elite Journal of Haematology*, *2*(3), 58-66.
14. Michel, J. B., & Martin-Ventura, J. L. (2020). Red blood cells and hemoglobin in human atherosclerosis and related arterial diseases. *International Journal of Molecular Sciences*, *21*(18), 6756.
15. Frimat, M., Boudhabhay, I., & Roumenina, L. T. (2019). Hemolysis derived products toxicity and endothelium: model of the second hit. *Toxins*, *11*(11), 660.
16. Doshi, H. U. (2021). *Clinical cases in obstetrics & gynecology*. Jaypee Brothers Medical Publishers.
17. Enosolease, M. E. (2021). Haematological Disorders in Pregnancy. *Contemporary Obstetrics and Gynecology for Developing Countries*, 363-373.
18. Obeagu, E. I., Adias, T. C., & Obeagu, G. U. (2024). Advancing life: innovative approaches to enhance survival in sickle cell anemia patients. *Annals of Medicine and Surgery*, *86*(10), 6021-6036.
19. Ganesh, B., Rajakumar, T., Acharya, S. K., & Kaur, H. (2022). Sickle cell anemia/sickle cell disease and pregnancy outcomes among ethnic tribes in India: an integrative mini-review. *The Journal of Maternal-Fetal & Neonatal Medicine*, *35*(25), 4897-4904.
20. Goonewardene, M., Shehata, M., & Hamad, A. (2012). Anaemia in pregnancy. *Best practice & research Clinical obstetrics & gynaecology*, *26*(1), 3-24.
21. Galadanci, A. A., Abdulqadir, I., Gwarzo, A. K., & Gume, S. A. (2019). Relationship between Folate Status and Complete Blood Count (CBC) Parameters in Sickle Cell Anaemia (SCA) at Steady State in Aminu Kano Teaching Hospital, Kano, Nigeria. *International Journal of Research and Reports in Hematology*, *2*(1), 74-79.
22. Obeagu, E. I., & Obeagu, G. U. (2024). Hypoxia in Pregnancy: Implications for Fetal Development. *Int. J. Curr. Res. Chem. Pharm. Sci*, *11*(7), 39-50.
23. Demirci, S., Leonard, A., Haro-Mora, J. J., Uchida, N., & Tisdale, J. F. (2019). CRISPR/Cas9 for sickle cell disease: applications, future possibilities, and challenges. *Cell Biology and Translational Medicine, Volume 5: Stem Cells: Translational Science to Therapy*, 37-52.
24. Asare, E. V., Olayemi, E., Boafor, T., Dei-Adomakoh, Y., Mensah, E., Ghansah, H., ... & Oppong, S. A. (2017). Implementation of multidisciplinary care reduces maternal mortality in women with sickle cell disease living in low-resource setting. *American journal of hematology*, *92*(9), 872-878.