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Review Article

Sickle cell Anemia

Abhinav Manish[1]*

[1]Dept. of Biochemistry, Gautam Buddha Chikitsa Mahavidyalaya, Dehradun, Uttarakhand, India.

Abstract

Sickle cell disease (SCD) is a monogenic disorder, yet its clinical presentation is influenced by a range of additional genetic and non-genetic factors. Despite decades of study, many aspects of the disease's genetic complexity remain unclear. Affecting millions globally, SCD is among the most common inherited blood disorders. Extensive research has identified both the primary genetic mutation and numerous modifier genes that affect disease severity. In recent years, significant progress has been made in understanding the molecular genetics, pathophysiology, and mechanisms behind symptom development and complications. Studies have explored cellular interactions, coagulation abnormalities, physiological changes, and links to other genetic conditions. Advances in screening—at the pre-conception, prenatal, and neonatal stages—have improved the ability to predict disease severity and clinical outcomes, helping reduce complications. Researchers have also investigated the influence of psychosocial and environmental factors on disease progression. Treatment strategies now include bone marrow and stem cell transplantation, with emerging therapies focusing on erythropoiesis regulation and gene editing. While SCD continues to carry a high risk of complications and mortality, ongoing developments in pharmacological treatments, gene therapy, and genetic modulation offer promising directions for more effective management. This review article is planned to cover the aspects of Sickle cell anemia which are known to us and try to find the gaps which are not discovered till yet and this review tried to focus on the current treatment modalities and futuristic treatment approaches for the sickle cell disease spectrum.

Keywords: Anemia, Hemoglobinopathies, Genotyping, Sickle cell Anemia, Sickle cell disease (SCD).

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1. Introduction

Sickle hemoglobinopathies represent a spectrum of hemoglobin genotypes, both common and rare, characterized by the presence of the sickle hemoglobin (HbS) mutation. Affected individuals may be homozygous for the HbS mutation (HBB: Glu6Val; GAG>GTG; rs334), resulting in sickle cell anemia—the most prevalent and severe form—or compound heterozygous, carrying HbS along with another globin gene mutation. Common compound heterozygous forms include HbSC disease (HbS and HbC mutations) and HbS-β thalassemia, which typically present with a milder clinical phenotype due to reduced intracellular HbS concentration.

This Mendelian disorder is primarily defined by two key features: vaso-occlusion and hemolytic anemia. Despite its monogenic origin, sickle hemoglobinopathies are known for their wide clinical and hematologic variability. Important genetic modifiers such as elevated fetal hemoglobin (HbF) levels and co-inherited α-thalassemia significantly influence disease severity, although additional genetic and environmental factors are also believed to play a role. The clinical characteristics and variability among different sickle hemoglobinopathies have been extensively reviewed in recent literature.[1]

2. Genetics and Molecular Basis

Hemoglobin is an essential protein within red blood cells that facilitates the transport of oxygen from the lungs to tissues across the body. Structurally, it is a quaternary protein composed of four globin subunits—two alpha (α) and two beta (β) chains—each housing a heme group where oxygen binds. These globin chains are intricately folded into specific three-dimensional shapes, featuring a hydrophobic interior and a hydrophilic exterior, which support their function in oxygen delivery. The heme group within each chain contains a central iron ion (Fe^{2+}) coordinated by four nitrogen atoms in a planar arrangement. This iron atom plays a critical role

*Corresponding author: Abhinav Manish
Email: Abhinav5manish@gmail.com

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in the reversible binding of oxygen. Hemoglobin's quaternary structure enables it to shift between two conformational states: the low-affinity "tense" (T) state and the high-affinity "relaxed" (R) state. This allosteric behavior allows hemoglobin to adjust its oxygen-binding affinity based on the body's needs, efficiently releasing oxygen in areas with increased demand, such as active muscles during exercise.[2]

Sickle cell trait and sickle cell disease are inherited conditions caused by mutations in the beta-globin gene (HBB). Individuals with sickle cell trait carry one normal beta-globin allele (HbA) and one mutated allele (HbS), whereas those with sickle cell disease inherit two copies of the HbS mutation (HbS/HbS). This mutation leads to the formation of abnormal hemoglobin, known as hemoglobin S, which can cause red blood cells to become stiff and adopt a sickle shape under low oxygen conditions.

These misshapen cells can block blood flow, resulting in a range of clinical complications. Both conditions follow an autosomal recessive inheritance pattern. People with only one copy of the HbS gene (heterozygotes) usually do not experience symptoms but can pass the gene to their children. When two carriers have a child, there is a 25% chance the child will inherit both mutated genes and develop sickle cell disease.

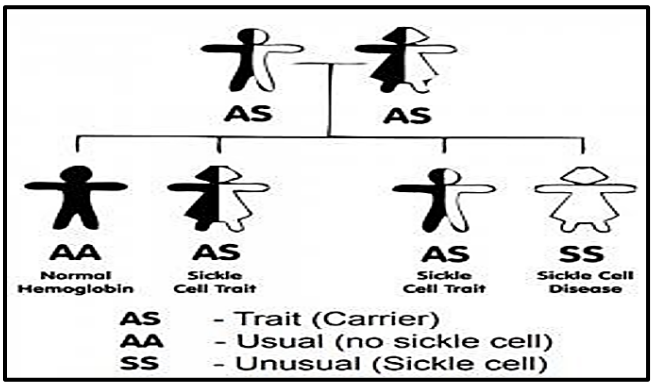

Fig 1: Sickle cell gene transmission from two carrier parents.

Ongoing research has identified several genetic factors that can modify the severity and presentation of sickle cell disease. These include elevated fetal hemoglobin (HbF) levels, co-inheritance of alpha-thalassemia, and other variations within the beta-globin gene cluster. Gaining a deeper understanding of these genetic influences is essential for improving diagnosis, providing effective genetic counseling, and developing targeted treatment strategies.[3]

Sickle hemoglobin polymerization occurs due to a genetic mutation in the beta-globin gene (HBB), resulting in the production of abnormal hemoglobin known as hemoglobin S (HbS). Under conditions of low oxygen levels, HbS molecules undergo a conformational change, causing them to aggregate and form long, insoluble polymers within the red blood cells. These polymers distort the shape of the cells, leading to the characteristic sickle shape and causing them to become rigid and prone to sticking to blood vessel walls, leading to vaso-occlusive events. The process of polymerization is initiated by the deoxygenation of HbS molecules, which promotes the exposure of hydrophobic patches on the surface of the protein. This allows the molecules to interact and aggregate, forming long, linear polymers. Once polymerization begins, it can propagate rapidly, especially in conditions of hypoxia or acidosis.Understanding the mechanisms of sickle hemoglobin polymerization is crucial for developing targeted therapies to prevent or inhibit this process and alleviate the symptoms of sickle cell disease.[4]

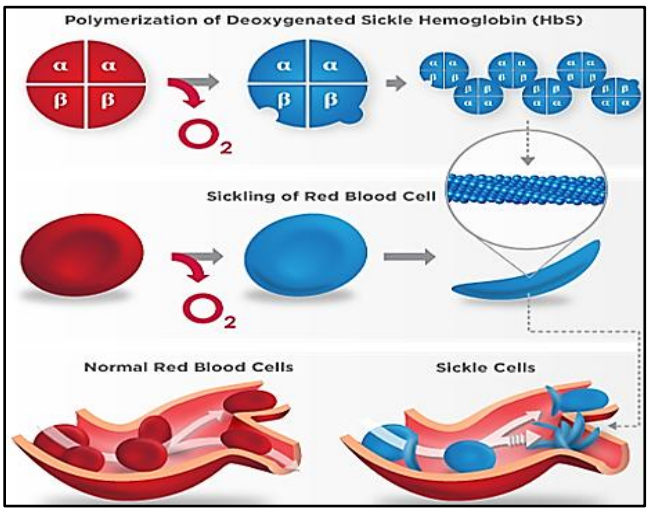

Fig 2: Mechanism of suckling in deoxygenated stage

3. Discussion

3.1. Pathophysiology

3.1.1. Vaso-occlusion and ischemia-reperfusion injury

Vaso-occlusion is a defining feature of sickle cell anemia (SCA), involving the blockage of blood vessels by abnormally shaped red blood cells, which impairs blood flow and causes tissue ischemia. When circulation is restored, reperfusion injury occurs, intensifying tissue damage through inflammation and oxidative stress. The sickled cells not only obstruct microvessels but also adhere to each other and to the vascular endothelium, triggering further vascular congestion, inflammation, and activation of the coagulation system. This interaction contributes to endothelial dysfunction, which worsens the cycle of occlusion and tissue injury. The ischemia-reperfusion process generates reactive oxygen species and promotes inflammatory responses, leading to organ damage and both acute and chronic complications in SCA. A deeper understanding of these mechanisms is critical for the development of therapies aimed at preventing or mitigating vaso-occlusive events and their long-term consequences.[5,6]

3.1.2. Chronic hemolysis and endothelial dysfunction

Chronic hemolysis and endothelial dysfunction are key pathophysiological features of sickle cell anemia (SCA) and contribute to its clinical manifestations and complications. Chronic hemolysis in SCA occurs due to the destruction of sickled red blood cells, Chronic hemolysis and endothelial dysfunction are central to the pathophysiology of sickle cell anemia (SCA) and play a major role in its associated complications. The persistent breakdown of sickled red blood cells releases free hemoglobin and heme into the bloodstream, which in turn reduces nitric oxide (NO) availability by binding to it. Since NO is a key vasodilator, its depletion leads to vascular constriction and impaired endothelial function. Moreover, the presence of cell-free hemoglobin and heme triggers oxidative stress, promotes inflammation, and activates coagulation pathways, all of which further damage the endothelium. Endothelial dysfunction in SCA is marked by reduced vasodilation, increased expression of adhesion molecules, heightened platelet activation, and a shift toward pro-inflammatory and pro-thrombotic conditions. These changes contribute to vaso-occlusion, tissue hypoxia, and progressive organ damage. Gaining insight into these interconnected mechanisms is crucial for the development of therapies aimed at reducing disease severity and improving clinical outcomes in SCA.[7,8]

3.1.3. Role of inflammation and oxidative stress

Inflammation and oxidative stress are key contributors to the pathogenesis and progression of sickle cell anemia (SCA), playing a significant role in its complications. Inflammatory responses in SCA involve the activation of leukocytes, platelets, and endothelial cells, resulting in elevated expression of adhesion molecules, release of pro-inflammatory cytokines, and recruitment of immune cells to areas affected by vaso-occlusion. This sustained inflammation promotes endothelial dysfunction and increases the binding of sickled red blood cells to blood vessel walls, leading to tissue damage and organ impairment. Concurrently, oxidative stress arises from excessive generation of reactive oxygen species (ROS) and a diminished antioxidant defense system. Hemolysis releases free hemoglobin and heme, which can undergo autoxidation and contribute to ROS formation, while ischemia-reperfusion cycles and ongoing inflammation further amplify oxidative stress. The accumulation of ROS causes cellular damage by oxidizing lipids, proteins, and DNA, thereby intensifying inflammation and tissue injury. Understanding the interplay between inflammation and oxidative stress is essential for developing effective treatments aimed at reducing disease severity and improving patient outcomes in SCA.[9,10]

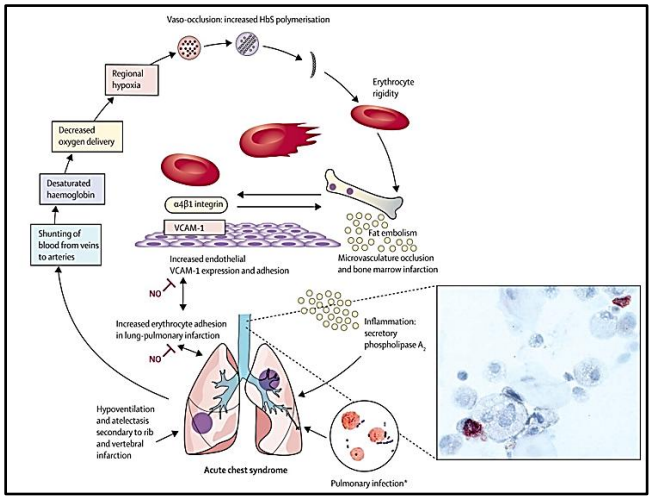

Fig. 3: Pathophysiology and clinical manifestations of sickle cell anemia

4. Clinical Manifestations

Sickle cell anemia (SCA) is associated with a wide range of clinical manifestations, affecting multiple organ systems. Here are some of the key clinical features:

1. Vaso-occlusive Crisis: Recurrent episodes of pain due to the obstruction of small blood vessels by sickled red blood cells, leading to tissue ischemia and infarction.
2. Anemia: Chronic hemolysis and reduced red blood cell lifespan lead to anemia, resulting in fatigue, weakness, and pallor.
3. Acute Chest Syndrome: Pulmonary complication characterized by chest pain, cough, dyspnea, and new infiltrates on chest imaging, often triggered by infection or vaso-occlusion in the lungs.
4. Stroke: Occlusion of cerebral blood vessels by sickled red blood cells can result in ischemic stroke, leading to neurological deficits.
5. Priapism: Prolonged painful erection due to vaso-occlusion in the penis, which can lead to erectile dysfunction and tissue damage if not promptly treated.
6. Splenic Sequestration: Sudden enlargement of the spleen due to pooling of sickled red blood cells, leading to abdominal pain, anemia, and potentially life-threatening hypovolemic shock.
7. Renal Complications: SCA can cause renal medullary infarction, renal papillary necrosis, and impaired kidney function, leading to hematuria, proteinuria, and renal failure.
8. Growth Delay and Delayed Puberty: Chronic anemia and nutritional deficiencies can lead to growth retardation and delayed onset of puberty in children with SCA.
9. Leg Ulcers: Chronic tissue ischemia and impaired wound healing predispose individuals with SCA to develop painful leg ulcers, particularly over bony prominences.
10. Gallbladder Disease: Pigment gallstones due to chronic hemolysis increase the risk of cholecystitis, biliary colic, and cholelithiasis.

5. Diagnosis and Screening

5.1. Newborn screening programs

Newborn screening programs for sickle cell anemia (SCA) involve testing infants shortly after birth to identify those with the disease or sickle cell trait. The screening typically involves a simple blood test, such as the heel prick test, to detect the presence of abnormal hemoglobin, particularly hemoglobin S (HbS). Early detection through newborn screening allows for timely initiation of preventive measures and interventions to reduce the risk of complications associated with SCA. These interventions may include parental education, vaccination against infections such as pneumococcus and meningococcus, initiation of prophylactic antibiotics, and early initiation of hydroxyurea therapy in infants identified with SCA. Newborn screening programs for SCA have been implemented in many countries worldwide, leading to improved outcomes and increased life expectancy for affected individuals. These programs have been shown to be cost-effective and beneficial in reducing morbidity and mortality associated with SCA.[11]

5.2. Diagnostic tests

Diagnostic tests for sickle cell anemia (SCA) include:

1. Hemoglobin Electrophoresis: This test separates different types of hemoglobin based on their charge and size, allowing for the detection of abnormal hemoglobin S (HbS) levels characteristic of SCA.
2. Sickle Solubility Test: A quick and inexpensive screening test that detects the presence of sickle hemoglobin by its insolubility in reducing agents.
3. High-Performance Liquid Chromatography (HPLC): This method quantifies the different types of hemoglobin present in a blood sample, including HbS, HbA, and fetal hemoglobin (HbF), providing a more precise measurement compared to hemoglobin electrophoresis.
4. Genetic Testing: Molecular genetic testing can identify specific mutations in the beta-globin gene (HBB), confirming the presence of SCA and distinguishing it from other hemoglobinopathies.
5. Complete Blood Count (CBC): This test measures the number of red blood cells, white blood cells, and platelets in the blood, providing information about anemia and potential complications such as leukocytosis or thrombocytosis.
6. Peripheral Blood Smear: Examination of a blood smear under a microscope can reveal characteristic sickle-shaped red blood cells, along with other morphological abnormalities.

These diagnostic tests play a crucial role in the identification and confirmation of SCA, guiding appropriate management and treatment strategies.[12]

5.3. Challenges and limitations in diagnosis

Diagnosing sickle cell anemia (SCA) presents several challenges and limitations, including:

1. Early Detection: Diagnosis in newborns can be challenging due to the need for specialized testing shortly after birth. In regions without newborn screening programs, SCA may not be detected until symptoms develop later in infancy or childhood.
2. Heterogeneity of Clinical Presentation: The clinical manifestations of SCA vary widely among individuals, making diagnosis based solely on symptoms challenging. Some individuals may have mild symptoms or be asymptomatic carriers, while others experience severe complications.
3. Overlap with Other Conditions: SCA shares clinical features with other hemoglobinopathies and hematological disorders, leading to potential misdiagnosis or delay in diagnosis. Distinguishing SCA from other forms of sickle cell disease or hemoglobinopathies requires specialized testing, such as hemoglobin electrophoresis or genetic testing.
4. Limited Access to Diagnostic Testing: In resource-limited settings, access to specialized diagnostic tests, such as hemoglobin electrophoresis or genetic testing, may be limited. This can result in underdiagnosis or misdiagnosis of SCA, particularly in regions with a high prevalence of the disease.
5. Genetic Complexity: SCA is caused by mutations in the beta-globin gene (HBB), but additional genetic modifiers can influence disease severity and phenotype. Genetic testing may not capture all relevant genetic variations, leading to incomplete characterization of disease risk and prognosis.
6. Stigma and Cultural Beliefs: Stigma associated with genetic diseases and cultural beliefs about SCA may contribute to delays in seeking medical care and reluctance to undergo diagnostic testing, particularly in communities where there is a lack of awareness or understanding of the disease.

6. Management and Treatment

Sickle cell anemia (SCA) is a genetic disorder characterized by abnormal hemoglobin, leading to the formation of sickle-shaped red blood cells. The management and treatment of SCA typically involve a combination of approaches aimed at preventing complications, managing symptoms, and improving overall quality of life. Here's a general protocol:

1. Education and Counseling: Provide comprehensive education to patients and their families about the nature of the disease, its inheritance pattern, symptoms, potential complications, and the importance of adherence to treatment plans. Counseling may also be necessary to address psychological and emotional aspects of living with SCA.
2. Hydroxyurea Therapy: Hydroxyurea is a medication that can help increase the production of fetal hemoglobin, which reduces the frequency of pain

crises and acute chest syndrome in patients with SCA. It is often prescribed to adults and children over a certain age.

3. Pain Management: Pain is a common symptom of SCA due to vaso-occlusion. Pain crises should be promptly managed with analgesic medications, hydration, and rest. Non-steroidal anti-inflammatory drugs (NSAIDs) and opioids may be used as needed, under careful supervision to avoid addiction.
4. Prevention of Infections: SCA patients are at an increased risk of infections, particularly pneumococcal infections. Vaccinations against pneumococcus, influenza, and other pathogens are essential. Antibiotic prophylaxis may also be recommended in certain cases.
5. Hydration: Adequate hydration is crucial for preventing sickling of red blood cells and reducing the risk of vaso-occlusive crises. Patients should be encouraged to drink plenty of fluids, especially during times of increased physical activity or in hot weather.
6. Transfusion Therapy: Red blood cell transfusions may be necessary to treat severe anemia, prevent stroke in high-risk individuals, or manage acute complications such as acute chest syndrome.
7. Folic Acid Supplementation: Folic acid supplementation is often recommended to support red blood cell production, as SCA patients have an increased rate of red blood cell turnover.
8. Regular Medical Follow-up: Patients with SCA require regular medical follow-up to monitor their condition, manage complications, and adjust treatment plans as needed. This may involve visits to hematologists, primary care physicians, and other specialists.
9. Chronic Disease Management: SCA is a chronic condition that requires ongoing management to prevent complications such as organ damage, stroke, and pulmonary hypertension. Regular monitoring of organ function, such as renal and cardiac function, is essential.
10. Psychosocial Support: Living with SCA can have a significant impact on the patient's quality of life. Psychosocial support services, including counseling and support groups, can help patients and their families cope with the emotional and social challenges associated with the disease.

This protocol should be tailored to the individual needs of each patient and may require modifications based on factors such as age, disease severity, and comorbidities. Close collaboration between patients, caregivers, and healthcare providers is essential for effectively managing SCA and optimizing patient outcomes.

6.1. Hematopoietic stem cell transplantation

Hematopoietic stem cell transplantation (HSCT) is a potential curative treatment for sickle cell anemia (SCA) that involves replacing the patient's defective hematopoietic stem cells with healthy ones from a compatible donor. Here's an overview of HSCT in the context of SCA.

1. Patient Selection: HSCT is typically considered for patients with severe SCA who have experienced complications such as frequent vaso-occlusive crises, acute chest syndrome, stroke, or severe anemia despite standard medical management. Patients must also have a suitable donor, usually a matched sibling or unrelated donor.
2. Pre-transplant Conditioning: Before undergoing HSCT, patients undergo a conditioning regimen, which may involve chemotherapy and/or radiation therapy. The purpose of conditioning is to suppress the patient's immune system and make space in the bone marrow for the donor stem cells.
3. Stem Cell Transplantation: Healthy hematopoietic stem cells from the donor are infused into the patient's bloodstream, where they migrate to the bone marrow and begin producing healthy blood cells, including red blood cells with normal hemoglobin.
4. Engraftment: Successful engraftment occurs when the donor stem cells establish themselves in the patient's bone marrow and begin producing new blood cells. This process typically takes several weeks, during which time the patient may be at risk of complications such as infections and graft failure.
5. Post-transplant Care: After HSCT, patients require close monitoring for complications such as graft-versus-host disease (GVHD), a condition in which the donor immune cells attack the recipient's tissues. Immunosuppressive medications are often prescribed to prevent or manage GVHD.
6. Long-term Follow-up: Long-term follow-up is essential to monitor the patient's progress, assess graft function, and manage any late complications or relapses. Patients may require ongoing medical care to address issues such as immunosuppression, organ toxicity, and infections.
7. Potential Benefits: HSCT offers the potential for a cure in selected patients with SCA, eliminating the need for ongoing transfusions, reducing the risk of complications such as stroke, and improving quality of life. However, the procedure carries risks, including transplant-related complications and the potential for graft rejection or relapse.
8. Risks and Considerations: HSCT is a complex and resource-intensive procedure associated with significant risks, including transplant-related mortality, graft failure, infections, and long-term complications such as infertility and secondary malignancies. Patient selection, donor compatibility, and careful pre-transplant evaluation are critical to optimizing outcomes.
9. Research and Advances: Ongoing research is focused on improving the safety and efficacy of HSCT for SCA, including alternative conditioning regimens, novel graft sources (such as haploidentical donors or cord blood), and strategies to reduce transplant-related complications.

HSCT can offer a potential cure for selected patients with severe SCA, but it is not without risks, and careful patient selection, pre-transplant evaluation, and post-transplant care

are essential to optimizing outcomes. Close collaboration between hematologists, transplant specialists, and other healthcare providers is crucial in managing patients undergoing HSCT for SCA.

7. Emerging Therapies and Research Directions

7.1. Gene therapy and gene editing approaches

1. Gene Therapy: Gene therapy involves introducing a functional copy of the hemoglobin gene into the patient's cells to produce normal hemoglobin. This is typically achieved using viral vectors, such as lent viruses or adeno-associated viruses, to deliver the therapeutic gene into the patient's hematopoietic stem cells. Once integrated into the genome, the therapeutic gene enables the production of normal hemoglobin, reducing or eliminating the symptoms of SCA.[13]
2. Gene Editing: Gene editing techniques, such as CRISPR-Cas9, enable precise modification of the defective hemoglobin gene in the patient's cells. In the context of SCA, gene editing aims to correct the specific mutation responsible for the production of abnormal hemoglobin S. CRISPR-Cas9 can be used to target and repair the mutated gene, restoring normal hemoglobin production and alleviating the symptoms of SCA.[14]

Both gene therapy and gene editing hold promise for providing a potentially curative treatment for SCA by addressing the underlying genetic cause of the disease. Clinical trials evaluating these approaches are ongoing, with encouraging results demonstrating the feasibility and safety of these innovative treatments.

8. Conclusion

Since the first description of the irregular sickle-shaped red blood cells (RBC) more than 100 years ago, our understanding of the disease has evolved tremendously. Recent advances in the field, more so within the last three decades, have alleviated symptoms for countless patients, especially in high-income countries. In 1984, Platt et al. first reported the use of hydroxyurea in increasing the levels of HbF. Since then, the treatment of sickle cell has taken to new heights by introducing several new agents (voxelotor, crizanlizumab, L-glutamine) and, most recently, gene therapy.[15]

In conclusion, sickle cell anemia (SCA) continues to pose a major global health burden, particularly in regions with high prevalence. While current treatment approaches primarily aim to manage symptoms, prevent complications, and enhance quality of life, there is increasing focus on therapies that target the genetic root of the disease. Emerging innovations such as gene therapy and gene editing are showing encouraging results in clinical trials, offering the potential for a lasting cure by correcting the faulty gene responsible for abnormal hemoglobin production. Hematopoietic stem cell transplantation (HSCT) remains a curative option for some individuals, with ongoing efforts to make it safer and more widely accessible. Additionally, research into disease-modifying therapies is advancing, targeting key mechanisms like red blood cell sickling, vascular dysfunction, inflammation, and oxidative stress. The rise of precision medicine also opens doors to more personalized care, allowing treatments to be tailored based on an individual's genetic makeup and disease severity.

On a broader scale, global health strategies focusing on prevention, early diagnosis, improved access to care, and public awareness are critical to addressing the worldwide impact of SCA. Ultimately, the future holds promise for transformative advances that may offer curative solutions and significantly enhance outcomes for those living with this challenging condition, underscoring the importance of sustained research, innovation, and healthcare investment.

9. Source of Funding

None.

10. Conflict of Interest

None.

References

1. Steinberg MH, Sebastiani P. Genetic modifiers of sickle cell disease. *Am J Hematol*. 2008;83(9):145–52. https;//doi:10.1002/ajh.23232
2. Perutz MF. Hemoglobin structure and respiratory transport. *Sci Am*. 1978;239(4):92-125. https;//doi:10.1038/scientificamerican1278-92
3. Weatherall DJ. The inherited diseases of hemoglobin are an emerging global health burden. *Blood.* 2010;115(22):4331-6. https;//doi:10.1182/blood-2010-01-251348
4. Eaton WA, Bunn HF. Treating sickle cell disease by targeting HbS polymerization. *Blood.* 2017;129(20):2719-26. https;//doi:10.1182/blood-2017-02-765891
5. Hebbel RP. Adhesive interactions of sickle erythrocytes with endothelium. *J Clin Invest.* 1997;100(11):S83-6.
6. Belcher JD, Chen C, Nguyen J. Heme triggers TLR4 signaling leading to endothelial cell activation and vaso-occlusion in murine sickle cell disease. *Blood.* 2014;123(3):377-90. https;//doi:10.1182/blood-2013-04-495887
7. Rees DC, Williams TN, Gladwin MT. Sickle-cell disease. Lancet. 2010;376(9757):2018-31. https;//doi:10.1016/S0140-6736(10)61029-X
8. Belcher JD, Chen C, Nguyen J. Heme triggers TLR4 signaling leading to endothelial cell activation and vaso-occlusion in murine sickle cell disease. *Blood.* 2014;123(3):377-90. https;//doi:10.1182/blood-2013-04-495887.
9. Belcher JD, Beckman JD, Balla G, et al. Inhaled carbon monoxide reduces leukocytosis in a murine model of sickle cell disease. *Am J Physiol Heart Circ Physiol.* 2005;288(6):H2771-9. https;//doi:10.1152/ajpheart.00327.2009
10. Aslan M, Ryan TM, Adler B. Oxygen radical inhibition of nitric oxide-dependent vascular function in sickle cell disease. *Proc Natl Acad Sci U S A.* 2001;98(26):15215-20. https;//doi:10.1073/pnas.221292098
11. Therrell BL, Lloyd-Puryear MA, Eckman JR. Newborn screening for sickle cell diseases in the United States: a review of data spanning 2 decades. *Semin Perinatol.* 2015;39(3):238-51. https;//doi:10.1053/j.semperi.2015.03.008

12. Bain BJ. Diagnosis from the blood smear. *N Engl J Med*. 2005;353(5):498-507. https;//doi:10.1056/NEJMra043442
13. Esrick EB, Bauer D.E. Genetic Therapies for Sickle Cell Disease. Seminars in Hematology, 2019;56(4):266–75. https://doi.org/10.1053/j.seminhematol.2019.07.002
14. Frangoul H, Altshuler D, Cappellini MD, Chen YS, Domm J, Eustace BK. et al. CRISPR-Cas9 Gene Editing for Sickle Cell Disease and β-Thalassemia. New Engl J Med. 2021;384(3):252–60. https://doi.org/10.1056/NEJMoa2031054.
15. Mangla A, Agarwal N, Maruvada S. Sickle Cell Anemia. 2023. In: StatPearls. Treasure Island (FL): StatPearls Publishing; 2025.

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