ETHIOPIAN INTERNATIONAL JOURNAL OF MULTIDISCIPLINARY RESEARCH

eISSN: 2349-5715 pISSN: 2349-5707

Volume: 12, Issue 05, May-2025 SJIF 2019: 4.702 2020: 4.737 2021: 5.071 2022: 4.919 2023: 6.980 2024: 7,662

# CURRENT MANAGEMENT STRATEGIES FOR THALASSEMIA MAJOR AND THALASSEMIA MINOR

***Tojiddinov Kh.S.***

*Andijan State Medical Institute*

*Republic of Uzbekistan, Andijan*

**Abstract:**Thalassemia is a group of inherited blood disorders characterized by reduced or absent synthesis of one or more of the globin chains that make up hemoglobin. Thalassemia major and thalassemia minor represent the severe and mild ends of the clinical spectrum, respectively. While thalassemia major demands lifelong medical management, including regular blood transfusions and iron chelation therapy, thalassemia minor is typically asymptomatic and may require minimal clinical intervention. Advances in diagnostics, treatment protocols, and supportive care have significantly improved patient outcomes. This article reviews the current management strategies for both thalassemia major and minor, highlighting differences in clinical approach, the role of genetic counseling, and future directions in curative therapies such as bone marrow transplantation and gene therapy.

**Keywords:**Thalassemia major, thalassemia minor, hemoglobinopathies, blood transfusion, iron chelation, gene therapy, bone marrow transplant, genetic counseling, beta-thalassemia

**INTRODUCTION:** Thalassemia is a hereditary blood disorder caused by mutations in the genes responsible for producing hemoglobin, the iron-containing protein in red blood cells that carries oxygen throughout the body. This disorder results in the abnormal formation or reduced production of one of the globin chains—either alpha (α) or beta (β)—leading to anemia of varying severity. Based on the type of affected globin chain, thalassemias are classified into alpha-thalassemia and beta-thalassemia. The clinical presentation varies widely depending on the number and type of defective genes inherited. **Thalassemia major** (also known as transfusion-dependent thalassemia or Cooley's anemia) is the most severe form. Individuals with this condition usually exhibit symptoms within the first two years of life, including severe anemia, poor growth, bone deformities, and splenomegaly. Without regular medical intervention, thalassemia major is often fatal during early childhood. Management of this condition includes lifelong blood transfusions, iron chelation therapy to counteract iron overload from transfusions, and supportive treatments to manage complications. Advanced therapies such as hematopoietic stem cell transplantation and gene therapy offer potential cures but are limited by accessibility and cost.

In contrast, **thalassemia minor** (also called thalassemia trait) is a much milder form of the disease. Individuals with thalassemia minor typically inherit one normal and one mutated gene. They may exhibit no symptoms or present with mild microcytic anemia that is often misdiagnosed as iron-deficiency anemia. Most people with thalassemia minor lead normal lives and do not require active medical treatment. However, its public health implications are significant due to its silent carrier status; two carriers can produce a child with thalassemia major. Hence, genetic counseling and screening are crucial components of managing thalassemia at a population level. Thalassemia is prevalent in many parts of the world, particularly in the Mediterranean region, South and Southeast Asia, the Middle East,

eISSN: 2349-5715 pISSN: 2349-5707

Volume: 12, Issue 05, May-2025 SJIF 2019: 4.702 2020: 4.737 2021: 5.071 2022: 4.919 2023: 6.980 2024: 7,662

and parts of sub-Saharan Africa. Global migration has increased the incidence in previously low-prevalence regions, making thalassemia a growing concern in diverse healthcare settings.

Over the years, advancements in molecular diagnostics, transfusion safety, iron chelation drugs, and curative therapies have significantly improved outcomes for individuals with thalassemia major. Simultaneously, better awareness and genetic counseling have improved reproductive decision-making for individuals with thalassemia minor. Despite these strides, challenges remain in ensuring access to care, especially in resource-poor settings.

## LITERATURE REVIEW

Thalassemia has been the focus of extensive research due to its global prevalence and the clinical challenges it poses. The literature reveals a clear distinction in the management strategies between thalassemia major and minor, with the former requiring intensive lifelong care and the latter necessitating mostly preventive and diagnostic interventions. This review synthesizes findings from peer-reviewed studies, clinical trials, and expert guidelines on the management of both conditions. Regular blood transfusions are the foundation of thalassemia major management, helping to correct severe anemia and suppress ineffective erythropoiesis. According to the Thalassemia International Federation (TIF) guidelines, maintaining pre-transfusion hemoglobin levels between 9–10.5 g/dL is essential for optimal growth and development [1]. However, chronic transfusions lead to secondary iron overload, which, if left untreated, causes damage to vital organs such as the liver, heart, and endocrine glands.

Iron chelation therapy is thus a critical adjunct to transfusion therapy. Deferoxamine (DFO) was the first widely used chelator but requires subcutaneous infusion, reducing patient compliance. Oral chelators like deferasirox (DFX) and deferiprone (DFP) have improved convenience and outcomes. A multicenter study by Cappellini et al. (2006) showed that DFX significantly reduced liver iron concentration and serum ferritin levels in transfusion-dependent patients, with acceptable safety profiles [2]. Additionally, long-term use of deferiprone has shown particular efficacy in reducing cardiac iron, which is a leading cause of mortality in thalassemia major [3]. HSCT remains the only established curative treatment for thalassemia major. The success of this therapy depends on the patient's age, iron load, and the availability of an HLA-matched sibling donor. Lucarelli et al. (1992) introduced a risk stratification model that predicts transplant outcomes based on these factors [4]. In a 2014 review, Angelucci et al. reported overall survival rates exceeding 80% in low-risk pediatric patients undergoing HSCT, with lower rates in older patients and those with advanced organ damage [5]. However, the high cost, risk of graft-versus-host disease (GVHD), and limited donor availability restrict the broader application of HSCT. Moreover, its utility in thalassemia intermedia and minor is not indicated, as these conditions do not warrant such intensive treatment.

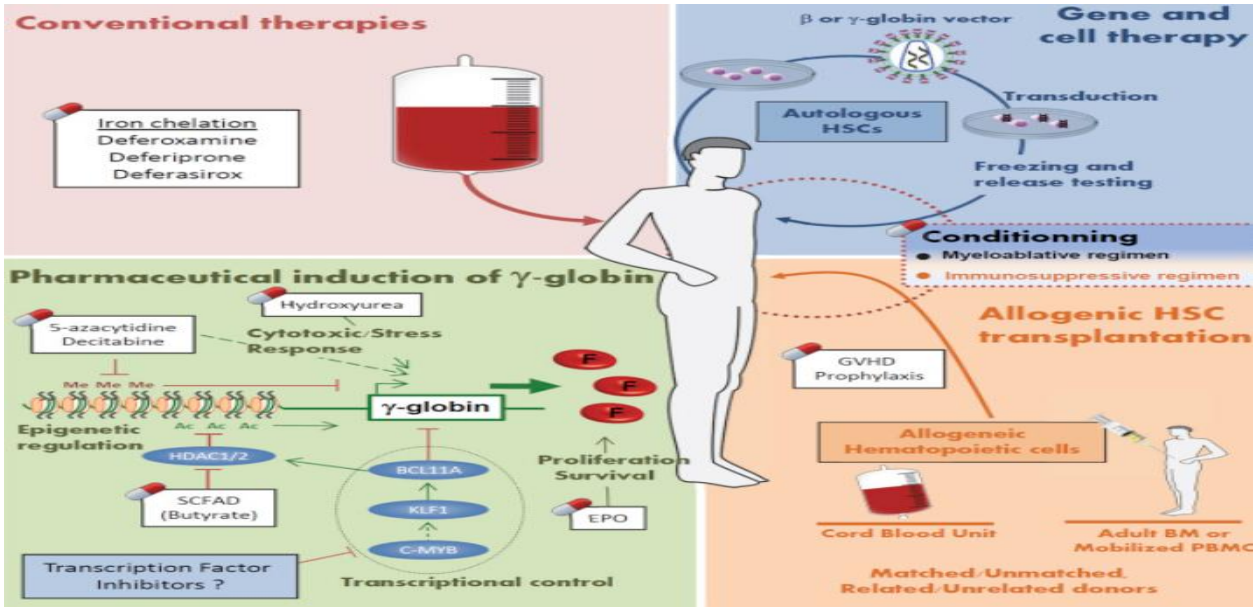
## ANALYSIS AND RESULTS

Thalassemia presents a complex spectrum of hematological disorders, with clinical severity ranging from mild asymptomatic anemia in thalassemia minor to life-threatening transfusion-dependent anemia in thalassemia major. Analyzing the current management approaches for both conditions reveals stark contrasts not only in clinical intervention but also in long-term patient care, outcomes, and public health strategies. In thalassemia major, also known as transfusion-dependent

eISSN: 2349-5715 pISSN: 2349-5707
Volume: 12, Issue 05, May-2025 SJIF 2019: 4.702 2020: 4.737 2021: 5.071 2022: 4.919 2023: 6.980 2024: 7,662

thalassemia, the primary therapeutic goal is to maintain effective hemoglobin levels to ensure normal growth, development, and physiological function. Regular blood transfusions remain the cornerstone of care. These transfusions are typically administered every 2 to 4 weeks to maintain pre-transfusion hemoglobin levels above 9 to 10.5 g/dL, preventing the complications associated with chronic anemia such as bone deformities, growth retardation, extramedullary hematopoiesis, and organ dysfunction. Transfusions provide immediate correction of anemia and help suppress ineffective erythropoiesis and skeletal abnormalities caused by marrow expansion. However, chronic transfusions lead to progressive iron accumulation, as the human body lacks a physiological mechanism to excrete excess iron. Each unit of transfused blood contains approximately 250 mg of elemental iron, and without intervention, this excess iron is deposited in various organs, including the liver, heart, and endocrine glands. This results in iron overload complications such as liver cirrhosis, cardiac failure, hypogonadism, diabetes, and hypothyroidism. To counteract this, iron chelation therapy is initiated, typically after 10–20 transfusions or when serum ferritin exceeds 1000 ng/mL.

Three main iron chelators are currently in clinical use. The first, deferoxamine, is administered parenterally (subcutaneously or intravenously), often overnight for 8–12 hours five to seven days a week. Despite its effectiveness, poor compliance due to the burdensome mode of administration limits its long-term success. To address this, oral chelators such as deferasirox and deferiprone were developed. Deferasirox, a once-daily oral chelator, is widely used due to its convenience and efficacy in reducing liver iron concentration. Deferiprone, taken three times daily, has shown superior effectiveness in removing cardiac iron. For some patients, especially those with severe iron overload or poor response to monotherapy, combination therapy using deferoxamine and deferiprone is employed. This dual approach targets both hepatic and myocardial iron, improving survival, particularly in patients with early signs of cardiac siderosis. Alongside transfusion and chelation therapy, patients undergo regular monitoring for organ function, iron levels, and complications. MRI T2* imaging is the gold standard for assessing myocardial and hepatic iron burden and has dramatically improved early detection of iron-induced cardiomyopathy, allowing for timely intervention. Endocrine assessments, including glucose tolerance tests, thyroid function, and pubertal hormone panels, are regularly performed due to the high incidence of iron-induced endocrine disorders.



eISSN: 2349-5715 pISSN: 2349-5707

Volume: 12, Issue 05, May-2025 SJIF 2019: 4.702 2020: 4.737 2021: 5.071 2022: 4.919 2023: 6.980 2024: 7,662

Beyond supportive care, curative approaches have gained momentum. Hematopoietic stem cell transplantation (HSCT) is the only well-established curative option currently available for thalassemia major. Ideally performed in children under ten years of age, HSCT offers the highest success rates in those without significant organ damage and with a matched sibling donor. Advances in conditioning regimens, improved HLA typing, and supportive care have enhanced transplant outcomes. Nevertheless, HSCT is limited by the availability of suitable donors, the risk of graft-versus-host disease, and the financial burden, especially in low-resource settings. Additionally, for adult patients or those with high-risk disease profiles, the procedure carries increased risks of morbidity and mortality. In recent years, gene therapy has emerged as a groundbreaking therapeutic modality for thalassemia major. By introducing a functional beta-globin gene into the patient's hematopoietic stem cells via lentiviral vectors or editing the genome to reactivate fetal hemoglobin production, gene therapy addresses the underlying genetic defect. Patients undergoing successful gene therapy have achieved transfusion independence or significantly reduced transfusion requirements. These outcomes represent a monumental shift in treatment paradigms, offering a potential lifelong cure. Nonetheless, this approach remains in early clinical adoption stages, with challenges related to accessibility, affordability, long-term safety, and technical standardization. High costs, infrastructure requirements, and regulatory complexities currently confine gene therapy to specialized centers in high-income countries.

In parallel to these clinical strategies, comprehensive supportive care is essential for managing complications and improving quality of life. Splenectomy, once common in reducing transfusion needs, is now approached with caution due to the associated risk of infections and thrombosis. When indicated, patients must receive appropriate vaccinations and prophylactic antibiotics. Nutritional support, folate supplementation, and psychosocial counseling form integral aspects of care. As life expectancy has improved, attention has shifted to quality-of-life issues, with increasing emphasis on education, employment support, and mental health interventions for adolescents and adults living with thalassemia. The scenario for thalassemia minor is markedly different. Individuals with thalassemia minor usually carry one mutated globin gene and exhibit no or only mild anemia. Often diagnosed incidentally during routine complete blood counts, these individuals show microcytic, hypochromic red blood cells with normal or slightly reduced hemoglobin levels. Importantly, the condition does not progress to thalassemia major or intermedia, and affected individuals typically have a normal life expectancy and no requirement for medical treatment.

## CONCLUSION

The management of thalassemia, both major and minor, requires a comprehensive, individualized, and context-sensitive approach. Thalassemia major, characterized by severe anemia and a lifelong dependency on transfusions, presents significant challenges that demand regular and coordinated medical care. Core management strategies—such as blood transfusions, iron chelation therapy, and close monitoring of organ function—have drastically improved survival and quality of life in affected individuals. Curative options like hematopoietic stem cell transplantation offer hope for long-term remission, while gene therapy is ushering in a new era of treatment possibilities that may redefine the standard of care in the coming years. On the other hand, thalassemia minor, although clinically mild, carries profound implications from a genetic and public health standpoint. Its asymptomatic nature often leads to underdiagnosis or mismanagement, particularly in populations where iron deficiency anemia is common. Proper identification and genetic counseling are crucial, not

eISSN: 2349-5715 pISSN: 2349-5707

Volume: 12, Issue 05, May-2025 SJIF 2019: 4.702 2020: 4.737 2021: 5.071 2022: 4.919 2023: 6.980 2024: 7,662

only for the well-being of the individual but also for reducing the risk of transmitting severe forms of the disease to future generations. National screening programs and public education have demonstrated their value in curbing the birth rate of thalassemia major, highlighting the power of preventive strategies in the broader fight against hereditary hemoglobinopathies.

**REFERENCES:**

1. Thalassemia International Federation. (2021). Guidelines for the Management of Transfusion Dependent Thalassaemia (TDT) – 3rd Edition. TIF Publications.
2. Cappellini, M. D., Cohen, A., Piga, A., Bejaoui, M., Perrotta, S., Agaoglu, L., ... & Vichinsky, E. (2006). A phase 3 study of deferasirox (ICL670), a once-daily oral iron chelator, in patients with β-thalassemia. Blood, 107(9), 3455-3462. [https://doi.org/10.1182/blood-2005-08-3430]
3. Pennell, D. J., Porter, J. B., Cappellini, M. D., & El-Beshlawy, A. (2006). Deferiprone for the treatment of iron overload in heart and liver: 1-year results from an international clinical trial. Blood, 107(9), 3738-3744.
4. Lucarelli, G., Galimberti, M., Polchi, P., Angelucci, E., Baronciani, D., Giardini, C., ... & Durazzi, S. M. (1992). Bone marrow transplantation in thalassemia. The New England Journal of Medicine, 326(7), 417-421.
5. Angelucci, E., Matthes-Martin, S., Baronciani, D., Bernaudin, F., Bonanomi, S., Cappellini, M. D., ... & Dalle, J. H. (2014). Hematopoietic stem cell transplantation in thalassemia major and sickle cell disease: indications and management recommendations from an international expert panel. Bone Marrow Transplantation, 49(6), 825–831.
6. Thompson, A. A., Walters, M. C., Kwiatkowski, J., Rasko, J. E., Ribeil, J. A., Hongeng, S., ... & Leboulch, P. (2018). Gene therapy in patients with transfusion-dependent β-thalassemia. The New England Journal of Medicine, 378(16), 1479-1493.