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Short Communication

Thalassemia in the 21st Century: Challenges, and Solutions, a Review Article

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Abstract

Thalassemia is among the most common inherited hemoglobin disorders worldwide, caused by mutations that impair the production of alpha or beta globin chains, resulting in chronic hemolytic anemia and significant morbidity. Advances in supportive care, such as regular blood transfusions and iron chelation therapy, have dramatically improved survival, yet iron overload, cardiac failure, endocrine dysfunction, and infections remain major complications. This review summarizes the current understanding of the genetic basis, pathophysiology, diagnosis, and evolving treatment options of thalassemia.

Keywords: thalassemia; hemoglobinopathy; iron overload; gene therapy; carrier screening

Introduction

Thalassemia represents a group of inherited disorders characterized by defective hemoglobin synthesis, leading to ineffective erythropoiesis and hemolytic anemia. The disease is most prevalent in the Mediterranean, Middle East, Indian subcontinent, and parts of Southeast Asia and Africa. It is caused by mutations that affect the production of either alpha (α) or beta (β) globin chains, resulting in alpha- or beta-thalassemia, respectively [1].

Genetic Basis and Pathophysiology

Thalassemia is typically inherited in an autosomal recessive manner. Beta-thalassemia results from mutations in the HBB gene on chromosome 11, leading to reduced (β^+) or absent (β^0) production of beta-globin chains. In alpha-thalassemia, gene deletions in HBA1 and HBA2 on chromosome 16 impair alpha-chain production.

The imbalance between alpha and beta chains causes ineffective erythropoiesis and hemolysis. In beta-thalassemia major, the complete absence of beta-globin leads to severe anemia that manifests in infancy and necessitates lifelong transfusion therapy [2].

Clinical Features

Thalassemia presents with a broad clinical spectrum:

- Thalassemia major: Severe transfusion-dependent anemia, hepatosplenomegaly, bone deformities, growth retardation, and iron overload complications.
- Thalassemia intermedia: Moderate anemia, variable transfusion needs, and fewer complications.
- Thalassemia minor: Usually asymptomatic with mild microcytic anemia.

Complications include cardiac failure, endocrine dysfunction, osteoporosis, and increased susceptibility to infections, particularly in patients who have undergone splenectomy [3].

Diagnosis

The diagnostic approach includes:

1. Complete Blood Count (CBC): Shows microcytic, hypochromic anemia with low MCV and MCH [4].
2. Peripheral Blood Smear: Reveals target cells, anisopoikilocytosis, and nucleated red cells.
3. Hemoglobin Electrophoresis or HPLC:
    - Beta-thalassemia major: High HbF, absent or low HbA.
    - Beta-thalassemia trait: Elevated HbA2 (>3.5%).
4. Genetic Testing: Confirms mutation type; useful for prenatal diagnosis and family screening.
5. *Serum Ferritin and MRI: Evaluate iron overload [5][6].

Management

1. Blood Transfusions

- Essential for patients with thalassemia major which should be performed in specialized centers.
- Aims to maintain Hb levels >9–10 g/dL.
- Risks: iron overload, alloimmunization, transmission of infections.

2. Iron Chelation Therapy

Iron overload from transfusions is managed using:

- Deferoxamine: Subcutaneous infusion.
- Deferiprone and Deferasirox: Oral agents with better compliance.

Chelation is guided by serum ferritin and organ-specific iron measurements [7].

3. Splenectomy

Considered for patients with hypersplenism or high transfusion requirements. It increases infection risk, necessitating vaccination against pneumococcus, meningococcus, and *Haemophilus influenzae* type b [8, 9].

4. Hematopoietic Stem Cell Transplantation (HSCT)

- The only curative option.
- Best results in young patients with HLA-matched sibling donors [10].

5. Emerging Therapies

- Gene therapy: Lentiviral vector-mediated transfer of functional beta-globin genes has shown success in trials [11].
- Luspatercept: Promotes late-stage erythroid maturation; reduces transfusion burden in transfusion-dependent patients [12].

Prevention and Screening

In high-prevalence areas, prevention strategies are critical:

- Carrier screening and genetic counseling.
- Premarital screening programs (e.g., in Cyprus and Iran) have significantly reduced disease incidence.
- Prenatal diagnosis via chorionic villus sampling or amniocentesis [13].

Community education plays a vital role in promoting these programs, especially in regions where consanguinity is common.

Complications: Without adequate management, thalassemia may result in:

- Iron overload: Cardiac dysfunction, hepatic fibrosis, diabetes, hypothyroidism.
- Infections: Particularly post-splenectomy.
- Skeletal deformities: Due to bone marrow expansion.
- Endocrine disorders: Including hypogonadism, delayed puberty, and growth failure [14].

Conclusion

Thalassemia remains a significant global health issue, especially in low-resource settings. While advances in chelation therapy, supportive care, and curative treatments like HSCT and gene therapy have improved survival and quality of life, prevention through carrier screening and public education remains the most cost-effective strategy. Coordinated care involving hematologists, endocrinologists, and infectious disease specialists is vital for optimal outcomes.

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