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Thalassemia: A lifelong battle with hemoglobin deficiency

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Abstract

Thalassemia is a heterogeneous group of inherited disorders of haemoglobin caused by reduced or absent production of one or more of the globin chains. They are the commonest single gene disease worldwide. The disease was first described by Thomas Cooley (a paediatrician from Detroit, USA) in 1925. the two common types, majority of β thalassaemias are caused by point mutations, while most of the α thalassaemias result from gene deletions.The resulting imbalance in globin synthesis is responsible for the ineffective erythropoiesi sand hemolysis typically observed in the thalassemia syndromes.About 3.2 % of the world's population (152 million people) carry β-thalassemia genes.The initial symptoms of the disease appear in the latter half of the first year of life, when the synthesis of γ-chains is not replaced by the synthesis of β-chains.The improved survival of patients with thalassemia major has been attributed to improvement in transfusion therapy, better understanding of mechanisms of organ damage from iron, more effective iron chelation, the availability of magnetic resonance for the evaluation of cardiac iron overload, and the referral of patients to centers of excellence.

Keywords: Thalassemia; Hemoglobin; Alpha-thalassemia; Beta-thalassemia; Anemia; Genetic Disorders; Blood Transfusions; Iron Chelation; Bone Marrow Transplant; Prognosis; Genetic Screening

1. Introduction

1.1. Thalassemia Syndromes

Thalassemia syndromes are a group of inherited hematological disorders characterized by reduced or absent synthesis of one or more globin subunits that constitute normal human hemoglobin (Hb). The most common forms include α-, β-, γ-, and δβ-thalassemia. According to the latest Bulletin of the World Health Organization, thalassemia mutations (2013) pose a significant public health burden, affecting 71% of 229 nations globally. It is estimated that approximately 1.5% of the global population carries genetic mutations that impair hemoglobin production.

1.2. Geographical Distribution

Thalassemia gene mutations are predominantly found across a broad geographical region extending from the Mediterranean basin through the Middle East, the Indian subcontinent, Burma, Southeast Asia, Melanesia, and the Pacific Islands. A-thalassemia is particularly prevalent in Southeast Asia (e.g., China, Thailand, Vietnam, Malaysia, and the Philippines), the eastern Mediterranean, and parts of the Middle East. In contrast, it is less common in Africa and India; however, α+ thalassemia is relatively more frequent in India.

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Thalassemia Prevalence and Estimated Affected Numbers

Region/Country	Prevalence (Estimated Carrier Rate)	Number of Affected People (Thalassemia Major)	Reference Year
Greece	5-9% of the population are carriers	~1,000 new cases annually	2020 (WHO)
Italy	3-4% of the population are carriers	~2,500-3,000 individuals with thalassemia major	2019 (WHO)
Cyprus	17% of the population are carriers	~100 new cases annually	2020 (Thalassemia International Federation)
India	3-4% of the population are carriers	Over 50,000 individuals with thalassemia major	2023 (WHO)
Pakistan	5-8% of the population are carriers	Over 10,000 new cases annually	2022 (Thalassemia International Federation)
Bangladesh	3-5% of the population are carriers	Around 10,000 individuals with thalassemia major	2021 (WHO)
China	2-4% of the population are carriers	Over 50,000 affected individuals	2020 (Thalassemia International Federation)
Turkey	2-5% of the population are carriers	~1,000 new cases annually	2019 (Thalassemia International Federation)
Iran	3-5% of the population are carriers	Around 20,000 affected individuals	2021 (WHO)
Saudi Arabia	2-3% of the population are carriers	~2,000 new cases annually	2020 (Thalassemia International Federation)
Thailand	5-8% of the population are carriers	7,000-10,000 affected individuals	2020 (WHO)
Egypt	6-8% of the population are carriers	~10,000 individuals with thalassemia major	2021 (WHO)
United States	0.2-1% of the population are carriers	Around 100,000 carriers, but fewer cases of thalassemia major	2020 (Thalassemia International Federation)
United Kingdom	1-2% of the population are carriers	10,000-15,000 affected individuals	2020 (WHO)

Figure 1 Prevalence of thalassemia major in different countries

The high prevalence of thalassemias, alongside sickle-cell disease and glucose-6-phosphate dehydrogenase (G6PD) deficiency, in malaria-endemic regions is likely due to the protective advantage heterozygous carriers possess against Plasmodium falciparum malaria. Mutations affecting the α- and β-globin genes are highly variable, with distinct frequencies across countries and regions. Even within specific countries, variations in migration patterns and the prevalence of consanguineous marriages have led to differences in the distribution of thalassemic mutations.

1.3. Pathophysiology of α-Thalassemia

The underlying defect in α-thalassemia is an imbalance in globin chain synthesis, causing an excess of β- and/or γ-globin chains. Unlike the unstable α-globin chains, excess γ-globin chains during fetal life and excess β-globin chains in postnatal life form soluble tetramers: γ4 (Hb Bart) and β4 (HbH), respectively. These tetramers, although soluble, impair red blood cell (RBC) function and stability, leading to hemolysis and, to a lesser extent, ineffective erythropoiesis.

Despite the identification of over 100 α-thalassemia mutations, clinical manifestations are categorized into four phenotypes of increasing severity: silent carrier, α-thalassemia trait, HbH disease, and Hb Bart hydrops fetalis.

- Four-Gene Deletion (Hb Bart Hydrops Fetalis): Involves the deletion of all four α-globin genes (both alleles on both chromosomes), resulting in complete absence of α-globin chain synthesis.

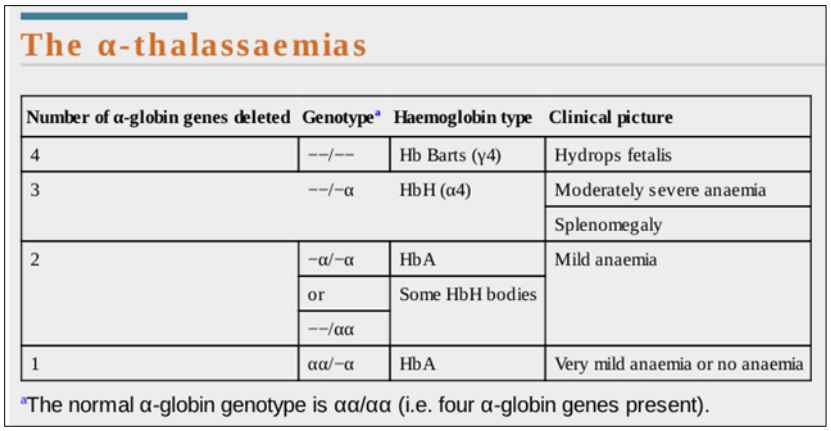
Only γ4 tetramers (Hb Bart) are produced, which cannot transport oxygen effectively. The condition is incompatible with life, leading to intrauterine death (stillbirth at 28–40 weeks) or death shortly after birth.

- Three-Gene Deletion (HbH Disease): Characterized by a severe reduction in α-globin chain synthesis. Results in the production of β4 tetramers (HbH) alongside reduced levels of HbA and Hb Bart. HbH is ineffective for oxygen transport and precipitates in erythrocytes and erythroblasts, leading to moderate anemia (hemoglobin levels 70–100 g/L) and splenomegaly, a presentation consistent with thalassemia intermedia.

Most individuals are not transfusion-dependent. HbA2 levels are typically normal or reduced.

- Two-Gene Deletion (α-Thalassemia Trait): Causes mild microcytosis with or without minimal anemia. HbH inclusion bodies may be observed in a peripheral blood smear stained with brilliant cresyl blue.
- One-Gene Deletion (Silent Carrier): Typically, asymptomatic with a normal blood picture.

Reference: The alpha Thalassaemia (Fessas P, Loukopoulos D, Kaltsoya A. Peptide analysis of the inclusions of erythroid cells in beta thalassemia. Biochim Biophys Acta. 1966; 124:430-432)



The α-thalassaemias

Number of α-globin genes deleted	Genotype[a]	Haemoglobin type	Clinical picture
4	−−/−−	Hb Barts (γ4)	Hydrops fetalis
3	−−/−α	HbH (α4)	Moderately severe anaemia
			Splenomegaly
2	−α/−α	HbA	Mild anaemia
	or	Some HbH bodies	
	−−/αα		
1	αα/−α	HbA	Very mild anaemia or no anaemia

[a]The normal α-globin genotype is αα/αα (i.e. four α-globin genes present).

Figure 2 The alpha Thalassaemias

1.4. B-Thalassemia

B-Thalassemia refers to a group of inherited disorders characterized by reduced or absent synthesis of the β-globin chains of hemoglobin, leading to imbalanced globin chain production. The resulting accumulation of unpaired α-globin chains causes hemolysis, ineffective erythropoiesis, and varying degrees of anemia. B-Thalassemia is classified into three clinical forms: β-thalassemia major, β-thalassemia intermedia, and β-thalassemia minor, depending on the severity of clinical presentation and transfusion requirements.

1.5. B-Thalassemia Major

B-Thalassemia major, also known as Cooley's anemia or Mediterranean anemia, represents the most severe form of the disorder. It results from homozygosity or compound heterozygosity for β-thalassemic mutations. Clinically, it is characterized by severe transfusion-dependent anemia requiring more than eight red blood cell transfusions annually.

The major pathological features of β-thalassemia major include:

- Severe Anemia: Reduced hemoglobin synthesis due to absent or markedly decreased β-globin chain production.
- Shortened red cell lifespan caused by the precipitation of insoluble excess α-globin chains.
- Ineffective erythropoiesis resulting from erythroid precursor apoptosis.
- Relative folate deficiency.
    - Skeletal Abnormalities:Expansion of erythroid marrow leads to bone deformities, including distortion of the skull, facial bones, and long bones.
    - Splenomegaly:Significant spleen enlargement occurs due to extramedullary hematopoiesis and chronic hemolysis.
    - Red Cell Morphology:Peripheral blood smear shows marked microcytosis, hypochromia, target cells, and extensive anisopoikilocytosis (variations in size and shape).

- Hemoglobin F Persistence:Hemoglobin F (HbF, $\alpha_2\gamma_2$) remains elevated throughout life, as β-globin synthesis is severely impaired. Symptoms typically appear around 6 months of age when HbF levels begin to decline.
- Iron Overload (Hemosiderosis): Chronic hemolysis, ineffective erythropoiesis, and repeated blood transfusions cause generalized iron overload, leading to organ damage.

1.6. β-Thalassemia Intermedia

β-Thalassemia intermedia describes a milder form of the disease, characterized by moderate anemia (hemoglobin levels between 70–100 g/L) that does not necessitate regular blood transfusions. Symptoms are less severe, and transfusions may only be required intermittently, such as during periods of physiological stress.

The clinical presentation may result from:

- Milder Genotypes:Homozygosity for mild β^+ mutations that permit partial β-globin chain synthesis.Coinheritance of α-Thalassemia:
- Reduced α-chain production mitigates α/β-globin chain imbalance, alleviating ineffective erythropoiesis and hemolysis.Hereditary Persistence of Fetal Hemoglobin (HPFH).Increased γ-globin chain synthesis (HbF) helps compensate for the β-globin deficiency, reducing the impact of α-chain excess.

1.7. β-Thalassemia Minor

β-Thalassemia minor, or β-thalassemia trait, occurs in heterozygous individuals who inherit one mutated β-globin allele. It is typically asymptomatic or associated with mild clinical manifestations, including:

- Minimal hypochromic microcytic anemia.Elevated levels of hemoglobin A_2 (HbA_2, $\alpha_2\delta_2$), a minor hemoglobin component that becomes more prominent in β-thalassemia minor.

1.7.1. Pathophysiology of β-Thalassemia

The fundamental defect in β-thalassemia is the reduced or absent production of β-globin chains, leading to a relative excess of unpaired α-globin chains. The key pathological consequences include:

- Decreased Hemoglobin Production:Reduced β-globin chain synthesis results in overall lower hemoglobin levels.
- A-Globin Chain Imbalance:Unpaired α-globin chains precipitate in erythroid precursors and mature red blood cells, disrupting erythroid maturation and membrane integrityThe extent of α-chain accumulation determines the severity of clinical manifestations.
- Erythroid Damage:Excess α-globin chains lead to oxidative stress, apoptosis of erythroid precursors, and shortened red cell lifespan, resulting in hemolysis and ineffective erythropoiesis.

In β^+-thalassemia (partial β-globin synthesis), residual β-globin production helps reduce the severity of α-chain imbalance. Similarly, persistence of γ-globin chain synthesis in β-thalassemia intermedia partially compensates for the β-chain deficit, improving the clinical outcome.Overall, the degree of α/non-α globin chain imbalance determines the clinical severity of β-thalassemia, ranging from asymptomatic carriers to transfusion-dependent β-thalassemia major.

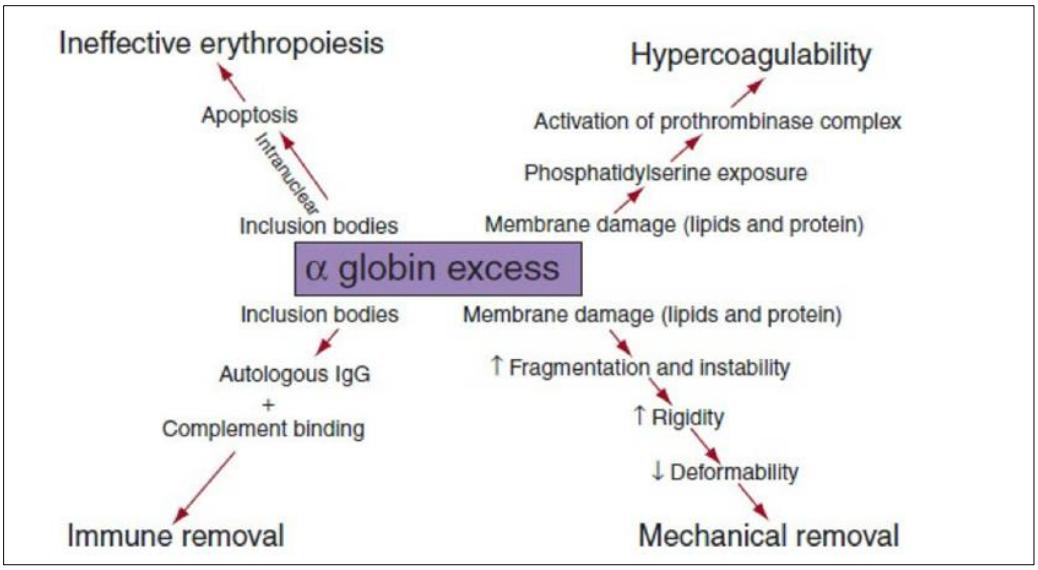


Figure 3 Pathophysiology of β-thalassemia. Ig, immunoglobulin. (Fessas P, Loukopoulos D, Kaltsoya A. Peptide analysis of the inclusions of erythroid cells in beta thalassemia. Biochim Biophys Acta. 1966; 124:430-432)

1.8. Clinical Features of β-Thalassemia

In β-thalassemia, the transition from fetal hemoglobin (HbF, $\alpha_2\gamma_2$) to adult hemoglobin (HbA, $\alpha_2\beta_2$) occurs postnatally. Consequently, the anemia develops gradually during infancy, typically around 6 months of age, and progressively worsens.

1.9. Key Clinical Manifestations

1.9.1. Severe Anemia

Progressive anemia leads to symptoms such as pallor, fatigue, and failure to thrive in early childhood. Growth and *Developmental Delays* Retarded physical growth and failure to achieve developmental milestones are common.

1.9.2. Skeletal Abnormalities

Expansion of erythroid marrow causes skeletal deformities, including: Frontal bossing of the skull. Maxillary overgrowth, resulting in the characteristic "chipmunk facies."

1.9.3. Radiological Changes

These include widening of the diploic space of the skull, "hair-on-end" appearance on X-rays, cortical thinning, and widening of the medullary cavities of long bones, with a predisposition to pathological fractures.

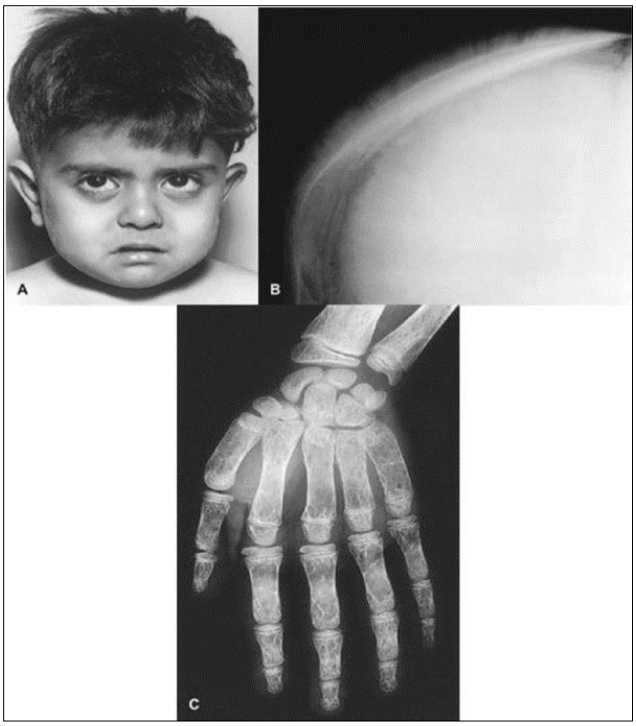


Figure 4 (A) Child with thalassaemia, showing the typical facial features. (B) Skull Xray of a child with β-thalassaemia, showing the 'hair-on-end' appearance. (C) X-ray of a hand, showing expansion of the marrow and a thinned cortex. (Courtesy of Dr. Orzincolo C, Castaldi G, Scutellari PN, Franceschini F. The beta-thalassaemia.Skeletal Radiol. 1989; 18:373-376.)

1.9.4. Hepatosplenomegaly

Enlargement of the liver and spleen occurs due to extramedullary hematopoiesis and chronic hemolysis.

1.9.5. Recurrent Infections

Increased susceptibility to infections is associated with iron overload, as elevated serum iron levels promote bacterial growth.

1.9.6. Iron Overload Complications

Chronic iron overload, resulting from repeated transfusions and hemolysis, can lead to systemic complications, including: Growth retardation, Skin hyperpigmentation., Hepatic damage progressing to cirrhosis, Endocrine dysfunction, such as insulin-dependent diabetes mellitus, delayed puberty, hypoparathyroidism, and hypothyroidism, Cardiac failure due to myocardial iron deposition.

1.9.7. Folate Deficiency

The increased erythroid turnover in β-thalassemia often results in relative folate deficiency

1.10. Screening for Thalassemia

Screening is an essential preventive strategy, particularly during antenatal care:

- Maternal Screening: All pregnant women should be screened during their first antenatal visit.
- Paternal Screening: If the mother is identified as a carrier, the father is screened to assess the risk of severe thalassemia in the fetus.
- Prenatal Diagnosis: Chorionic Villus Sampling (CVS): Performed at ≥10 weeks of gestation, CVS provides fetal DNA for genetic analysis using advanced methods such as PCR, Southern blotting, or RFLP analysis.
- Fetal Blood Sampling: Conducted at 18 weeks of gestation for analysis of globin chain synthesis.

- Preimplantation Genetic Diagnosis: Embryonic biopsy allows for genetic analysis before implantation, reducing the risk of affected pregnancies.

1.11. Laboratory Features

- *Peripheral Blood Examination:*Severe microcytic hypochromic anemia with hemoglobin levels ranging from 2 to 6 g/dL.Red blood cells exhibit marked anisopoikilocytosis, target cells, basophilic stippling, Howell-Jolly bodies, and nucleated red cells on blood smear examination.
- *Test for Inclusion Bodies:*Aggregates of unpaired α-globin chains can be visualized in erythroblasts using supravital staining (e.g., methyl violet). Post-splenectomy, these inclusion bodies may also appear in peripheral blood.
- *Hemoglobin Electrophoresis:*Elevated levels of HbF (ranging from 10% to 98%).HbA_2 may be normal or mildly elevated.In homozygous β^0-thalassemia, HbA is absent; in β^+/β^+ or β^0/β^+ forms, reduced levels of HbA are detected.
- *Bone Marrow Examination:*Shows marked erythroid hyperplasia, indicative of ineffective erythropoiesis.
- *Iron Studies:*Increased serum iron and ferritin levels.Unconjugated bilirubin is elevated due to hemolysis.
- Osmotic Fragility:Decreased red cell osmotic fragility is noted.

B-Thalassemia major represents a significant public health concern, particularly in regions surrounding the Mediterranean, the Middle East, and Southeast Asia. In resource-limited settings, inadequate transfusion support and iron chelation therapy result in poor survival rates and reduced quality of life.

B-Thalassemia Major: Without regular blood transfusions and iron chelation therapy, affected infants rarely survive beyond early childhood. Inadequate treatment leads to severe complications, including iron overload and organ dysfunction.

B-Thalassemia Intermedia: Represents a milder phenotype where regular transfusions are not required, but patients may experience anemia-related symptoms and growth retardation.

1.12. Principles of Therapy

1.12.1. Blood Transfusion

Historically, transfusions were administered only when anemia became symptomatic. This “on-demand” approach resulted in skeletal deformities, hepatosplenomegaly, and poor survival.The hypertransfusion protocol was developed to maintain hemoglobin levels ≥9.5–10 g/dL. Regular transfusions help suppress ineffective erythropoiesis, prevent skeletal deformities, and improve quality of life.

1.12.2. Iron Chelation Therapy

Chronic transfusions result in iron overload, which requires chelation therapy to prevent organ damage.Desferrioxamine (DFO): Administered subcutaneously via infusion pumps (25–60 mg/kg/day) for 12 hours, 5–6 days per week, often combined with vitamin C to enhance iron excretion.

1.12.3. Bone Marrow Transplantation (BMT)

BMT is the only curative option for β-thalassemia major, though it carries significant risks of morbidity and mortality.

The decision to pursue BMT depends on a careful assessment of individual risk-benefit profiles.

Reference: Properties of iron chelating drugs used in thalassaemia. (Cohen AR, Glimm E, Porter JB. Effect of transfusional iron intake on response to chelation therapy in beta-thalassemia major. Blood. 2008; 111:583-587.)

Table 1 Properties of iron chelating drugs

Parameter	Desferrioxamine	Deferiprone	Deferasirox
1. Molecular weight	657 Da	139 Da	373 Da
2. Iron:chelator binding ratio	1:1	1:3	1:2
3. Plasma ½ life	20–30 min	1.5–3.5 hr	12–18 hr
4. Route of administration	Parenteral (SC/IV)	Oral	Oral
5. Daily dose	25–50 mg/kg 5 days a week	75 mg/kg three times daily	20–30 mg/kg once daily
6. Route of iron excretion	Urine and faeces	Urine	Faeces
7. Side effects	Impaired vision or hearing, growth retardation	Gastrointestinal upset, arthralgia, agranulocytosis	Gastrointestinal upset, rashes, raised serum creatinine

1.13. Prevention of Thalassemia: Strategies and Priorities

Thalassemia prevention should be prioritized due to its significant health and economic burden. Effective strategies rely on public awareness, carrier screening, genetic counseling, and prenatal diagnosis.

1.13.1. Public Health Education

Raising awareness through mass communication platforms, such as media campaigns, helps educate the population about the nature of thalassemia, its socioeconomic impact, and the importance of preventive measures.

1.13.2. Carrier Screening and Genetic Counseling

Carrier screening involves identifying individuals who are heterozygous for thalassemia mutations through simple, cost-effective diagnostic tests.Genetic counseling plays a pivotal role in informing at-risk individuals about the genetic implications and risks of inheritance.It is strongly recommended that heterozygous carriers avoid marrying another carrier of the same thalassemia gene to reduce the likelihood of having offspring with severe disease.

1.13.3. Prenatal Diagnosis

Prenatal diagnosis is a critical intervention for couples at risk of having a child with thalassemia. It can be divided into two approaches:

- Retrospective Diagnosis: Performed in couples who already have an affected child.
- Prospective Diagnosis: Conducted in couples identified as carriers through screening programs.
- Advances in prenatal diagnostic techniques allow early detection of affected fetuses, enabling informed decisions, including the option of selective termination of pregnancy where permissible.
- By integrating health education, carrier screening, genetic counseling, and prenatal diagnostics into public health initiatives, the incidence of thalassemia can be effectively reduced.

1.14. prognosis

Thalassemia is a group of inherited blood disorders that impact hemoglobin production, resulting in anemia. The severity of the condition can vary widely based on the specific type of thalassemia, the mutations involved, and the age at which it is diagnosed. Prognosis for those with thalassemia is influenced by several factors, including the type of thalassemia, the availability of treatments, and how well complications are managed. Both alpha and beta thalassemia types often require regular blood transfusions, iron chelation therapy, and other medical interventions. If left untreated, thalassemia can lead to serious complications such as endocrine dysfunction (which may include growth retardation, hypothyroidism, and diabetes), splenomegaly (enlargement of the spleen), and hepatomegaly (enlargement of the liver). Additionally, bone deformities can occur due to increased erythropoiesis, which is the expansion of bone marrow.The outlook for individuals with thalassemia is contingent on various factors, including whether it is alpha or beta thalassemia, the severity of the condition, the age at which it is diagnosed, and the effectiveness of treatment.

2. Results

Thalassemias are inherited as autosomal recessive disorders. Hemoglobin A (HbA) is composed of two α-globin and two β-globin chains (α2β2). The synthesis of α-globin chains is regulated by two gene clusters located on chromosome 16, while β-globin chain production is controlled by genes on chromosome 11. Each globin gene contains three exons (coding sequences) and two introns (non-coding regions). The synthesis of both α- and β-globin chains is mediated by RNA transcription. Studies have consistently demonstrated that regular blood transfusions, combined with iron chelation therapy, significantly improve the quality of life and survival rates in patients with thalassemia. However, long-term management remains challenging due to complications such as iron overload, which can cause irreversible organ damage.

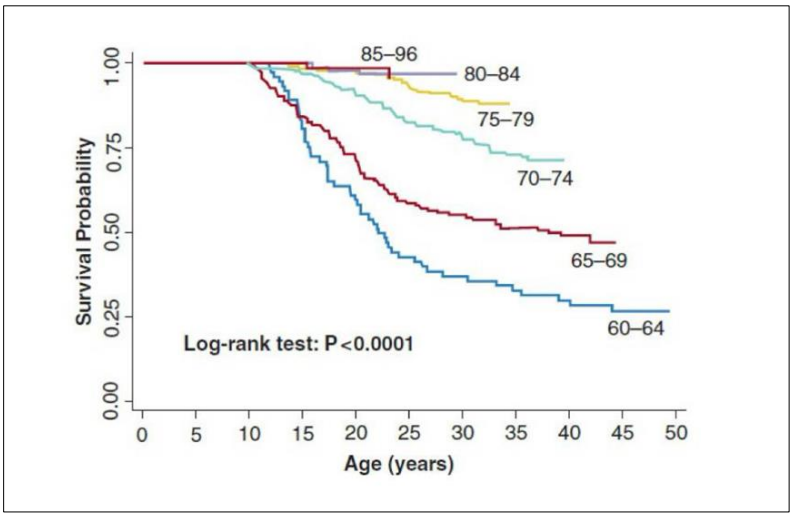


Figure 5 Kaplan-Meier survival curve after the first decade of life, subdivided by cohort of birth of patients from an Italian cooperative study. The survival data were collected in 2009. The role of the cohort of birth is evident

Bone marrow transplantation has emerged as a curative approach for some patients, though its widespread use is limited by the availability of suitable donors and the risks associated with the procedure. A large cooperative Italian study reported improved survival rates for patients born in recent years, with females exhibiting better outcomes compared to males. Despite these advancements, mortality rates in thalassemia patients remain elevated compared to the general population. Data from 2010 indicated that 68% of patients survived beyond 35 years of age, with heart disease accounting for 67% of deaths. Iron-induced oxidative damage remains a major contributor to complications in thalassemia, emphasizing the need for ongoing surveillance, infection prophylaxis, and early intervention. Chronic hepatitis, which is often observed in transfusion-dependent patients, should be appropriately managed. As survival rates continue to improve, new complications are emerging, shifting the clinical landscape of thalassemia and necessitating novel therapeutic strategies to address these evolving challenges.

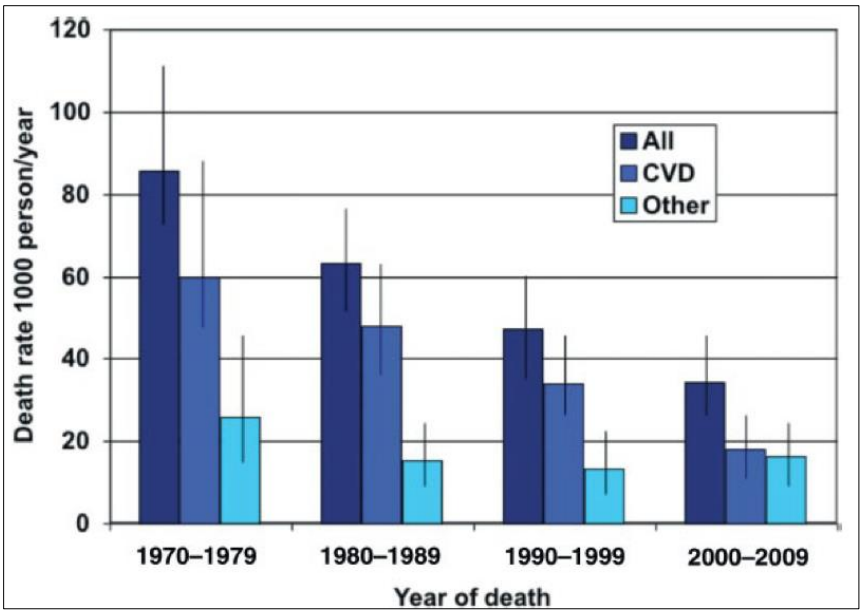


Figure 6 Decrease in death rate in a multitransfused population of Italian thalassemia patients by year at death. Death constantly decreased because of the decrease in cardiac causes. (Data collected in 2009 as part of the 7 Centers Study

3. Discussion

Thalassemia remains a substantial global health burden, particularly in regions where it is highly prevalent. Despite significant advancements in medical management, including blood transfusion programs, iron chelation therapy, and bone marrow transplantation, numerous challenges persist. Chronic iron overload continues to be a critical complication in thalassemia patients, necessitating lifelong treatment and vigilant monitoring to prevent organ damage. While bone marrow transplantation remains the only curative therapy currently available, it is associated with considerable risks, including morbidity and mortality, and is not universally accessible.

Emerging therapies, such as gene therapy, offer a promising avenue for a definitive cure. Preliminary clinical trials have shown encouraging results regarding safety and efficacy. However, these approaches remain experimental, and further research is essential to assess their long-term outcomes, scalability, and affordability.Another pressing concern is the disparity in healthcare accessibility. In low-resource settings, limited availability of diagnostic tools, regular transfusions, chelation therapy, and advanced treatments significantly hinders the management of thalassemia, exacerbating disease outcomes. Addressing these challenges through global health initiatives, improved healthcare infrastructure, and research efforts is crucial to mitigating the burden of thalassemia worldwide.

4. Conclusion

Thalassemia is a complex genetic disorder that continues to present significant health challenges globally. While a universal cure remains elusive, current treatment options—including regular blood transfusions, iron chelation therapy, and bone marrow transplantation—have significantly enhanced patient survival and quality of life. Emerging therapies, such as gene therapy, offer promising prospects for a definitive cure, though further research and clinical trials are required to establish their safety, efficacy, and long-term outcomes. Early diagnosis, comprehensive multidisciplinary care, and effective preventive measures remain critical for improving disease management and patient outcomes.

Reviews and Future Directions

Advancements in clinical research, improved access to healthcare, and the publication of observational studies have contributed to more accurate diagnosis and enhanced treatment protocols for thalassemia. However, disparities in healthcare systems, particularly in low-resource countries facing economic and sanitary challenges, result in divergent clinical outcomes.

Regular red blood cell transfusions combined with iron chelation therapy are the cornerstone of managing β-thalassemia major. Adherence to these treatments mitigates anemia, prevents hypoxia, and suppresses ineffective erythropoiesis, enabling patients to lead near-normal lives. Nonetheless, the long-term success of these therapies relies on consistent access to care and resources.

Improving healthcare infrastructure and ensuring equitable access to timely diagnosis and treatment in underserved regions are essential to addressing the global burden of thalassemia. International collaborations, research initiatives, and global health programs will be pivotal in advancing new therapeutic options and closing gaps in healthcare delivery. With sustained efforts, the prospects for managing and potentially curing thalassemia will continue to improve, offering hope for affected individuals worldwide.

Compliance with ethical standards

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Disclosure of conflict of interest

There is no conflict of interest in any of the statements present in the article.

References

[1] Weatherall DJ. The evolving spectrum of the epidemiology of thalassemia. Hematol Oncol Clin North Am. 2018, 32(2):165-175.

[2] Modell B, Darlison M. Global epidemiology of haemoglobin disorders and derived service indicators. Bull World Health Organ. 2008, 86:480-487.

[3] Williams TN, Weatherall DJ. World distribution, population genetics, and health burden of the hemoglobinopathies. Cold Spring Harb Perspect Med. 2012, 2:a011692.

[4] Galanello R, Eleftheriou A, Traeger-Synodinos J. Prevention of Thalassemia and Other Haemoglobin Disorders. Vol 1. Nicosia, Cyprus: Thalassemia International Federation, 2001.

[5] Higgs D, Buckle V, Gibbons R, Steensma D. Unusual types of alpha thalassemia. In: Steinberg M, Forget B, Higgs D, Weatherall D, eds. Disorders of Hemoglobin: Genetics, Pathophysiology and Clinical Management. Cambridge, England: Cambridge University Press, 2009:296-321.

[6] Cohen AR, Glimm E, Porter JB. Effect of transfusional iron intake on response to chelation therapy in beta-thalassemia major. Blood. 2008, 111:583-587.

[7] Orzincolo C, Castaldi G, Scutellari PN, Franceschini F. The “lamellated” skull in beta-thalassaemia. Skeletal Radiol. 1989, 18:373-376.

[8] Fessas P, Loukopoulos D, Kaltsoya A. Peptide analysis of the inclusions of erythroid cells in beta thalassemia. Biochim Biophys Acta. 1966, 124:430-432

[9] World Health Organization (WHO) – Thalassemia WHO provides global guidelines and an overview of thalassemia, including its treatment and management. 1990, 2001, 2008, 2020 (Thalassemia International Federation)

[10] De Gobbi M, Viprakasit V, Hughes JR, et al. A regulatory SNP causes a human genetic disease by creating a new transcriptional promoter. Science. 2006, 312:1215-1217.

[11] Fritsch EF, Lawn RM, Maniatis T. Molecular cloning and characterization of the human beta-like globin gene cluster. Cell. 1980, 19:959-972.

[12] Gonzalez-Redondo JM, Stoming TA, Kutlar A, et al. A C—T substitution at nt-101 in a conserved DNA sequence of the promotor region of the beta-globin gene is associated with "silent" beta-thalassemia. Blood. 1989, 73:1705-1711.

[13] Thein S, Wood W. The molecular basis of beta thalassemia, delta-beta thalassemia and hereditary persistence of fetal hemoglobin. In: Steinberg M, Forget B, Higgs D, Weatherall D, eds. Disorders of Hemoglobin: Genetics, Pathophysiology and Clinical Management. Cambridge, England: Cambridge University Press, 2009:323-356.

[14] Pirastu M, Ristaldi MS, Loudianos G, et al. Molecular analysis of atypical beta-thalassemia heterozygotes. Ann N Y Acad Sci. 1990, 612:90-97.

[15] Oggiano L, Guiso L, Frogheri L, et al. A novel Mediterranean "delta beta-thalassemia" determinant containing the delta (+) 27 and beta (0) 39 point mutations in cis. Am J Hematol. 1994, 45:81-84.

[16] Kulozik AE, Bellan-Koch A, Kohne E, Kleihauer E. A deletion/inversion rearrangement of the beta-globin gene cluster in a Turkish family with delta beta zero-thalassemia intermedia.Blood 1992, 79:2455-2459.

[17] MedlinePlus (National Institutes of Health) “Thalassemia.” National Library of Medicine, U.S. National Institutes of Health. Last updated: 2023. Source: MedlinePlus - Thalassemia.

[18] Mayo Clinic “Thalassemia.” Mayo Clinic, 2023. Source: Mayo Clinic - Thalassemia

[19] Thalassemia International Federation (TIF) Cappellini, M. D., Poggiali, E., & Vitiello, G. (2020). “Thalassemia: The Current State of the Art and Future Perspectives.” Hematology, 25(1), 1-8.

[20] Borgna-Pignatti, C., et al. (2010)“Survival and complications in patients with thalassemia major.”