Review on Current Status and Treatment Option of Thalassemia in Bangladesh

PROJECT REPORT

[In the partial fulfillment of the requirements for the degree of Bachelor of Pharmacy]

Submitted To

Department of Pharmacy

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Daffodil International University

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APPROVAL

This project paper, **"Review on Current Status and Treatment Option of Thalassemia in Bangladesh",** submitted to the Department of Pharmacy, Faculty of Allied Health Sciences, Daffodil International University, has been accepted as satisfactory for the partial fulfillment of the requirements for the degree of Bachelor of Pharmacy and approved as to its style and contents.

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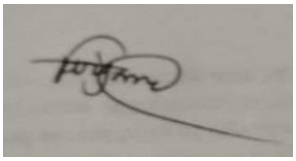
DECLARATION

I hereby declare that this project report, **"Review on Current Status and Treatment Option of Thalassemia in Bangladesh"** is done by me under the supervision of Ms. Farjana Islam Aovi Assistant Professor, I am declaring that this Project is my original work. I also declare that neither this project nor any part thereof has been submitted elsewhere for the award of Bachelor or any degree.

Supervised by



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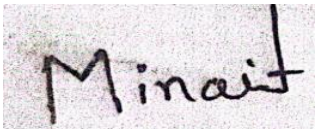

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My Parents,

The persons who always encourage me in every sphere of my life.

My teacher,

The persons who guided me in this process and the faculties who kept me on track.

Abstract

Thalassemia, a hereditary blood disorder characterized by abnormal hemoglobin production, poses significant health challenges in Bangladesh. This review aims to provide a comprehensive overview of the current status and treatment options available for thalassemia in the country. The review explores the epidemiology of thalassemia in Bangladesh, highlighting the high carrier rate and the socio-economic impact on affected families. Current treatment options, including blood transfusions, iron chelation therapy, and bone marrow transplantation, are critically examined. Additionally, the review discusses the emerging role of gene therapy and prenatal diagnosis in managing the disorder. Challenges such as limited healthcare resources, lack of awareness, and inadequate screening programs are identified, underscoring the need for comprehensive national strategies. Approximately 77.3% of patients were diagnosed with HbE beta thalassemia, while nearly 15% had beta thalassemia major. Around 41.1% of TDT patients required blood transfusions every 2-4 weeks. Due to incomplete medical records, transfusion history was missing for 115 diagnosed cases (approximately 9.7% of all cases). In our study, over 62% of HbE beta thalassemia patients were treated as TDT, while about 28% were NTDT. In Bangladesh, 85% of blood is donated by patients' relatives and friends, with the remaining 15% from voluntary donors. Studies indicate that the prevalence of HCV among frequently transfused thalassemia patients ranges from 3% to 67.3%. The review concludes by emphasizing the importance of public health initiatives, community education, and government support in improving the prognosis and quality of life for thalassemia patients in Bangladesh.

Table of Contents

List of Figures

Chapter 1
Introduction

1. Introduction

Thalassemia is a prevalent genetic blood disorder in Bangladesh, posing significant health challenges to the population. Characterized by the body's inability to produce adequate hemoglobin, thalassemia results in severe anemia and related complications. The disorder manifests in two main types: alpha and beta thalassemia, with beta thalassemia being more common and severe in Bangladesh. The high prevalence of thalassemia in Bangladesh can be attributed to various factors, including high carrier rates, lack of awareness, and consanguineous marriages [1]. Despite advances in medical science, the condition remains a significant public health concern, particularly due to limited resources and healthcare infrastructure. This review aims to provide a comprehensive overview of the current status of thalassemia in Bangladesh, including its epidemiology, genetic basis, and the socio-economic impact on affected individuals and families [2]. Additionally, it will explore the existing treatment options, ranging from blood transfusions and iron chelation therapy to emerging gene therapies and bone marrow transplants. By examining the challenges and advancements in thalassemia management, this review seeks to highlight the need for enhanced healthcare strategies and policies to improve the quality of life for those affected by this debilitating disorder in Bangladesh [3].

1.1 Etiology of Thalassemia

Thalassemia is a group of inherited blood disorders characterized by the body’s inability to produce adequate hemoglobin, leading to anemia. The etiology of thalassemia involves genetic mutations that affect the production of hemoglobin, the protein in red blood cells responsible for carrying oxygen throughout the body [4].

Types of Thalassemia

Alpha Thalassemia: Caused by mutations or deletions in the HBA1 and HBA2 genes, which code for the alpha-globin chains of hemoglobin. The severity depends on the number of gene deletions:

Silent Carrier: One gene deletion; usually asymptomatic.

Alpha Thalassemia Trait: Two gene deletions; mild anemia.

Hemoglobin H Disease: Three gene deletions; moderate to severe anemia, splenomegaly [5].

Alpha Thalassemia Major (Hydrops Fetalis): Four gene deletions; usually fatal before or shortly after birth.

Beta Thalassemia: Caused by mutations in the HBB gene, which codes for the beta-globin chains of hemoglobin. The severity depends on whether one or both genes are affected:

Beta Thalassemia Minor (Trait): One gene mutation; mild anemia.

Beta Thalassemia Intermedia: Two gene mutations; moderate anemia, possible need for occasional blood transfusions.

Beta Thalassemia Major (Cooley's Anemia): Two gene mutations; severe anemia, requiring regular blood transfusions and other treatments [6].

Genetic Inheritance

Thalassemia follows an autosomal recessive inheritance pattern, meaning a person must inherit two defective genes (one from each parent) to exhibit severe forms of the disease. Carriers (with one defective gene) are usually asymptomatic or have mild symptoms [7].

1.2 Pathogenesis of Thalassemia

Genetic Mutations

Alpha Thalassemia: Normally, four genes are involved in producing alpha-globin chains. Mutations can lead to:

Silent Carrier: One gene mutation, usually asymptomatic.

Alpha Thalassemia Trait: Two gene mutations, causing mild anemia.

Hemoglobin H Disease: Three gene mutations, leading to moderate to severe anemia.

Hydrops Feta’s: Four gene mutations, usually fatal in utero or shortly after birth.

Beta Thalassemia: Normally, two genes are involved in producing beta-globin chains [8].

Mutations can lead to:

Beta Thalassemia Minor: One gene mutation, causing mild anemia.

Beta Thalassemia Intermedia: Two gene mutations, resulting in moderate anemia.

Beta Thalassemia Major (Cooley's anemia): Severe mutations in both genes, leading to severe anemia requiring regular blood transfusions [9].

Hemoglobin Imbalance

The genetic mutations in thalassemia lead to an imbalance in the production of globin chains:

Excess Unpaired Globin Chains: The lack of sufficient alpha or beta chains results in an excess of the other type of chain. These unpaired chains form unstable tetramers that precipitate within the red blood cells [10].

Ineffective Erythropoiesis: The precipitation of unpaired globin chains damages the developing red blood cells in the bone marrow, leading to ineffective erythropoiesis (production of red blood cells).

Hemolysis: Damaged red blood cells are often destroyed prematurely, leading to hemolysis (destruction of red blood cells) and resulting in anemia [11].

Secondary Effects

Anemia and Hypoxia: The reduced oxygen-carrying capacity of the blood leads to tissue hypoxia (lack of oxygen), stimulating the bone marrow to produce more red blood cells. This compensatory mechanism results in bone marrow expansion and skeletal deformities.

Iron Overload: Regular blood transfusions, a common treatment for severe thalassemia, can lead to iron overload, as the body has no natural way to excrete excess iron. This can damage vital organs such as the heart, liver, and endocrine glands [12].

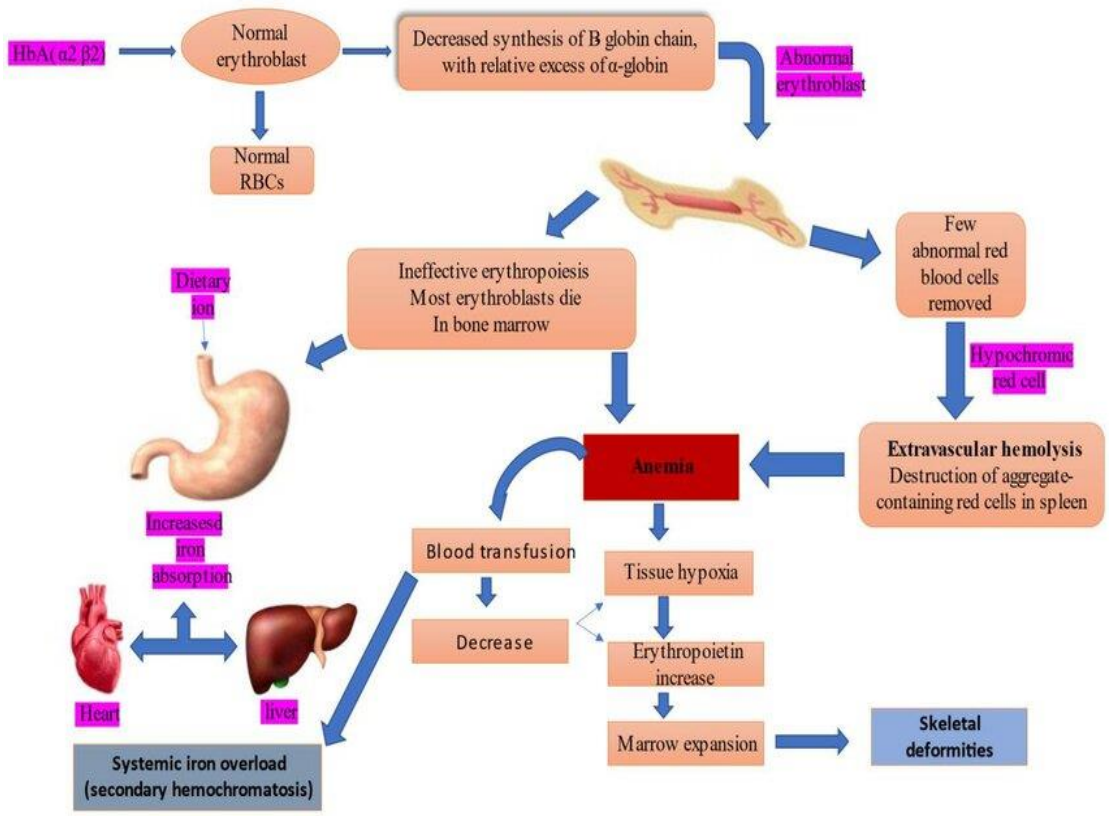

Figure 1: Pathogenesis of Thalassemia

1.3 Clinical Manifestations of thalassemia

Thalassemia is a group of inherited blood disorders characterized by reduced or absent synthesis of hemoglobin chains, leading to anemia and various systemic complications. The clinical manifestations of thalassemia vary widely depending on the type and severity of the genetic mutation [13]. There are two main forms: alpha-thalassemia and beta-thalassemia, each affecting the production of the alpha or beta globin chains, respectively. The severity of symptoms ranges from mild, asymptomatic forms to severe, life-threatening anemia requiring regular blood transfusions. Common clinical features include pallor, fatigue, and jaundice. In more severe cases, patients may present with growth retardation, skeletal deformities, splenomegaly, and iron overload complications. Understanding these clinical manifestations is crucial for the timely diagnosis and management of thalassemia, significantly improving patient outcomes [14].

1.4 Socioeconomic and Psychological Impact of thalassemia

Thalassemia, a genetic blood disorder, has significant socioeconomic and psychological impacts on affected individuals and their families. Here's an overview of these impacts:

Socioeconomic Impact

Healthcare Costs:

Direct Costs: Regular blood transfusions, iron chelation therapy, medications, and hospital visits are expensive. These costs can be a significant financial burden, especially in countries with limited healthcare funding [15].

Indirect Costs: Parents often miss work to care for their sick children, resulting in loss of income. In severe cases, one parent may have to give up their job entirely to provide full-time care.

Employment Challenges:

Individuals with thalassemia may face difficulties in finding and maintaining employment due to frequent medical appointments and health-related absences. Employers may also be reluctant to hire individuals with chronic health conditions [16].

Education Disruption:

Children with thalassemia often miss school due to hospital visits and illness, leading to gaps in their education and difficulties in keeping up with peers. This can impact their long-term educational and career prospects.

Social Stigma and Discrimination:

In some cultures, genetic disorders are stigmatized, leading to social isolation and discrimination. This can affect marriage prospects and social relationships [17].

Psychological Impact

Emotional Distress:

Constant medical procedures and the chronic nature of the illness can cause significant stress and anxiety for both patients and their families. Children with thalassemia may experience fear and distress related to frequent hospital visits and painful treatments.

Depression and Anxiety:

The chronic nature of the disease and the burden of treatment can lead to depression and anxiety. Patients may feel hopeless about their condition, and the uncertainty of their future can exacerbate these feelings [18].

Quality of Life:

Thalassemia can significantly impact the quality of life. Chronic fatigue, pain, and the need for constant medical care can limit the ability to participate in normal activities, leading to feelings of frustration and helplessness.

Family Dynamics:

The stress of caring for a chronically ill family member can strain family relationships. Siblings may feel neglected as parents focus their attention on the child with thalassemia, leading to feelings of resentment and jealousy [19].

Coping Mechanisms and Support

Support Groups and Counseling:

Psychological support through counseling and support groups can help patients and families cope with the emotional and psychological burden of the disease. Sharing experiences with others facing similar challenges can provide comfort and practical advice.

Educational Programs:

Educating families about thalassemia and its management can empower them to better handle the condition and reduce anxiety related to the unknown [20].

Financial Assistance Programs:

Government and non-governmental organizations can provide financial assistance to help families manage the costs associated with thalassemia treatment.

Community Awareness:

Increasing awareness about thalassemia can reduce stigma and discrimination, encouraging a more supportive and inclusive environment for affected individuals.

Addressing the socioeconomic and psychological impacts of thalassemia requires a comprehensive approach involving medical care, psychological support, financial assistance, and community education [21].

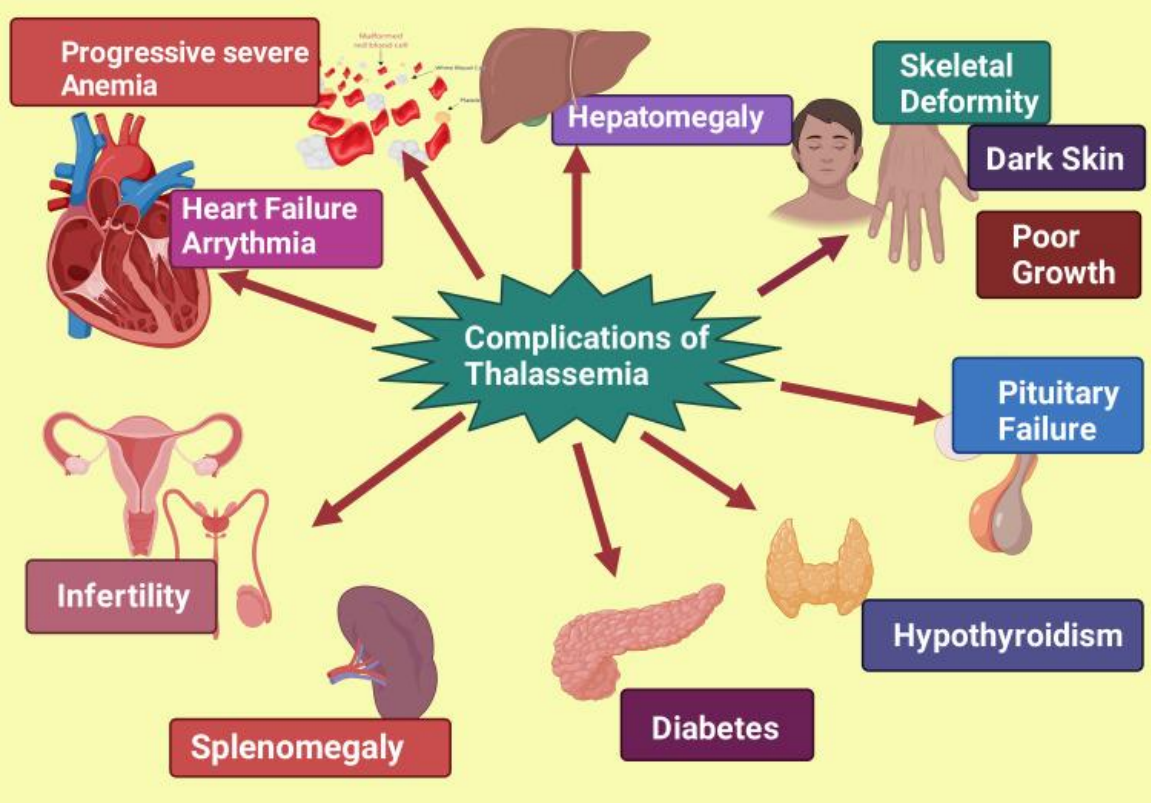

Figure 2: Showing the various complications of thalassemia

Chapter 2
Purpose of the study

2. Purpose of the study

The purpose of this study is to provide a comprehensive review of the current status and treatment options for thalassemia in Bangladesh. This involves:

- To assess the prevalence and distribution of different types of thalassemia.
- To review the existing diagnostic methods and their effectiveness in identifying thalassemia.
- To analyze the current treatment options available.
- To identify the major challenges faced by healthcare providers and patients in managing thalassemia.
- To review the national health policies, governmental and non-governmental programs.

Chapter 3
Literature Review

3.1 Literature Review

Analysis 1:

The lifespan and quality of life for patients with thalassemia have improved in industrialized countries. Despite these advancements, complications remain common, including heart disease (such as heart failure and arrhythmias), chronic liver hepatitis that can progress to cirrhosis and, in rare cases, hepatocellular carcinoma, endocrine issues (like hypogonadism, hypothyroidism, diabetes, hypoparathyroidism), stunted growth, osteoporosis, thrombophilia, and pseudoxanthoma elasticum. However, the occurrence of these complications is decreasing in younger patients due to the use of virus-screened blood transfusions and the introduction of new oral iron chelators and imaging techniques. Accurate measurement of iron deposits has enabled better management of iron overload. Furthermore, treatments for many of these complications are available. Specialized expertise in treating thalassemia patients is crucial [22].

Analysis 2:

Thalassemia's are some of the most common inherited diseases globally, affecting people from the Mediterranean, Middle East, Transcaucasia, Central Asia, Indian subcontinent, and Southeast Asia. Managing these diseases involves long-term care, making the prevention of the homozygous state a crucial strategy. This article examines major prevention programs established in several countries across Europe, Asia, and Australia, often inspired by initiatives in Sardinia. These extensive programs include carrier detection, molecular diagnostics, genetic counseling, and prenatal diagnosis. The variability in clinical severity is often due to interactions with α-thalassemia and mutations that boost fetal production. Currently, specialized methods like preimplantation and preconception diagnosis are costly and not widely available. However, recent successful studies on fetal DNA in maternal plasma suggest the potential for future noninvasive prenatal diagnosis [23].

Analysis 3:

β-thalassemia is a severe, inherited hemoglobin disorder caused by mutations in the HBB gene, presenting a significant global public health challenge. Despite limited comprehensive research in Bangladesh, worldwide prevalence and smaller studies suggest a high prevalence of this disease in the country. This review aims to investigate the current status of β-thalassemia in Bangladesh and suggest future mitigation strategies. Factors contributing to the high prevalence include limited awareness, high rates of consanguineous marriages, and insufficient access to healthcare, compounded by the lack of public health policy and national health insurance. The lack of comprehensive data on the mutation spectrum impedes understanding of the genetic landscape and modern treatment strategies for β-thalassemia. While conventional therapies like blood transfusion are available, advanced treatments such as splenectomy, hematopoietic stem cell transplantation, and emerging gene therapies are promising but not yet widely accessible in Bangladesh. Addressing the challenges of β-thalassemia requires comprehensive strategies, including public awareness campaigns, public health interventions, mandatory premarital screening, genetic counseling, and a national prevention program. Furthermore, understanding the mutation spectrum and exploring new therapeutic interventions are essential for advancing healthcare strategies [24].

Chapter 4
Methodology

4.1 Data collection procedure

Look for books, conference proceedings, peer-reviewed journals, and legal guidelines pertaining to **"Review on Current Status and Treatment Option of Thalassemia in Bangladesh"** To locate pertinent papers, reputable databases such as PubMed, Scopus, Google Scholar, and Research Gate have been utilized.

- It has been starting work for this in June 2024.
- Every effort has been made to gather as much information as possible by using search terms such as "Pathophysiology of Thalassemia," "Prevention of Thalassemia" "Management of Thalassemia," and "Etiology of Thalassemia". These terms were checked for potential exploits on educational bibliographic databases, web-based search engines, PubMed, Research Gate, Google Scholar, and Medline.
- An academic evaluation leads the inspection; about **30 publications** are examined for this evaluation.
- In an effort to streamline the process, compiling all data from **2000 to 2024** and all work completed in Microsoft Word.
- Each assessment paper that was created was reviewed, and it got even more scholarly. The gathered information has finally been distilled.

4.2 Data analysis strategy

Data analysis is the methodical application of statistical and/or logical tools for describing and illustrating, condensing and summarizing, and evaluating data. Microsoft Excel was used to analyses the data.

Chapter 5

Results & Discussion

5.1 Elements of Thalassemia Prevention

Public Awareness and Education: Raising awareness and education to health personnel, groups at risk, population at large and also among policymaker is the critical prerequisite for thalassemia prevention. Mass population education should be modulated according to the social values, religious laws and cultural characteristics of the country. In Srilanka, inspite of free facilities for thalassemia screening, uptake was very poor. So, their recommendation was more intensive monitoring and strengthening of education programs. Also recommend intensive education of health professionals as well as the population at large in the field of preventive measures of thalassemia [25].

Carrier detection and Premarital Screening: Several procedures have been proposed for thalassemia carrier detection18. These are CBC, Hb Electrophoresis and PCR based analysis. In South Asian rural area one tube fragility test associated with dichlorophenol indophenol (DCIP) dye test is used to detect the presence of Hb E, which is the most common in this region. Those individual who resulting positive at this screening test are further investigate by quantitative HbA2 determination for identifying heterozygous β-thalassemia. But, one tube fragility test may miss those β-thalassemia heterozygotes who coinherited with β−thalassemia [26]. A carrier detection procedure should be designed to avoid missing any couple at risk and their recommendation is quantitative evaluation of HbA2 for carrier detection, which may be obtained by electrophoresis or by high pressure liquid chromatography (HPLC). HPLC has the additional advantages to quantitate HbF and to detect clinical relevant Hb variants which may interact with β-thalassemia heterozygosity. Now a days, detection of the most frequent mutations or deletions of β-globin and β-globin gene are detected by a PCR based procedure among the most commonly used commercially available RDB (Reverse oligonucleotide hybridization) analysis and allele-specific amplification ARMS (Amplification refractory mutation system) analysis [27]. Now, in many countries premarital carrier screening is being performed on a voluntary basis. In Cyprus, the Orthodox Church requires a certificate providing that screening for thalassemia has been performed before marriage, but allows the final decision on marriage and reproduction option to be left to the couple. In a number of Muslim countries including Saudi Arabia, Iran, United Arab Emirates, Bahrain, Tunisia,

Lebanon, Qatar and Gaza Strip the national premarital program are mandatory and aimed at limiting carrier marriage [28].

Genetic Counseling to the couples at risk: Genetic counseling plays the most important part in thalassemia prevention program. A genetic counselor must be trained in molecular genetics of thalassemia and should have sufficient experience and expertise to communicate with and give detail information's about the disease to the patients and family members. According to international rules, counseling has been performed in a non-directive way but direct to the counselee's corner and is based on a private interview [29].

Prenatal Diagnosis: Thalassemia detection is possible directly by the analysis of amplified DNA collected from fetal trophoblastic or amniotic fluid cells. Now-a-days, prenatal diagnosis by DNA analysis is available in Mediterranean area (Cyprus, Sardinia, several regions of Continental Italy), Northern Europe (Netherland, Belgium and Germany), Northern and South America, Hongkong, Taiwan, China, Indonesia, Malaysia, Jordan. Prenatal diagnosis service has also been introduced even in many developing countries [30].

Table 1: An overview of the Preventive Measures for Thalassemia

Preventive Measure	Description	Reference
Genetic Counseling	Provides information and support to individuals or families about the genetic nature of thalassemia, inheritance patterns, and implications for family planning.	31
Carrier Screening	Identifies individuals who carry the thalassemia gene, particularly in populations with a high prevalence of the disorder.	
Prenatal Diagnosis	Involves testing the fetus for thalassemia through procedures like chorionic villus sampling (CVS) or amniocentesis, allowing parents to make informed decisions.	32
Pre-implantation Genetic Diagnosis	Used in conjunction with in vitro fertilization (IVF) to select embryos that do not carry the thalassemia gene, preventing the disorder from being passed to offspring.	

Public Awareness Campaigns	Educates the public about thalassemia, its genetic nature, and the importance of carrier screening and genetic counseling.	33
Premarital Screening	Encourages or mandates screening for thalassemia carriers before marriage, especially in high-prevalence areas, to prevent the birth of affected children.	
Newborn Screening	Early detection of thalassemia in newborns to initiate timely treatment and management, improving outcomes and quality of life.	34
Vaccination and Preventive Health	Ensures thalassemia patients receive appropriate vaccinations and preventive health measures to reduce complications associated with the disorder.	
Iron Chelation Therapy Education	Educates patients and families about the importance of iron chelation therapy in preventing iron overload due to frequent blood transfusions, a common treatment for thalassemia.	35

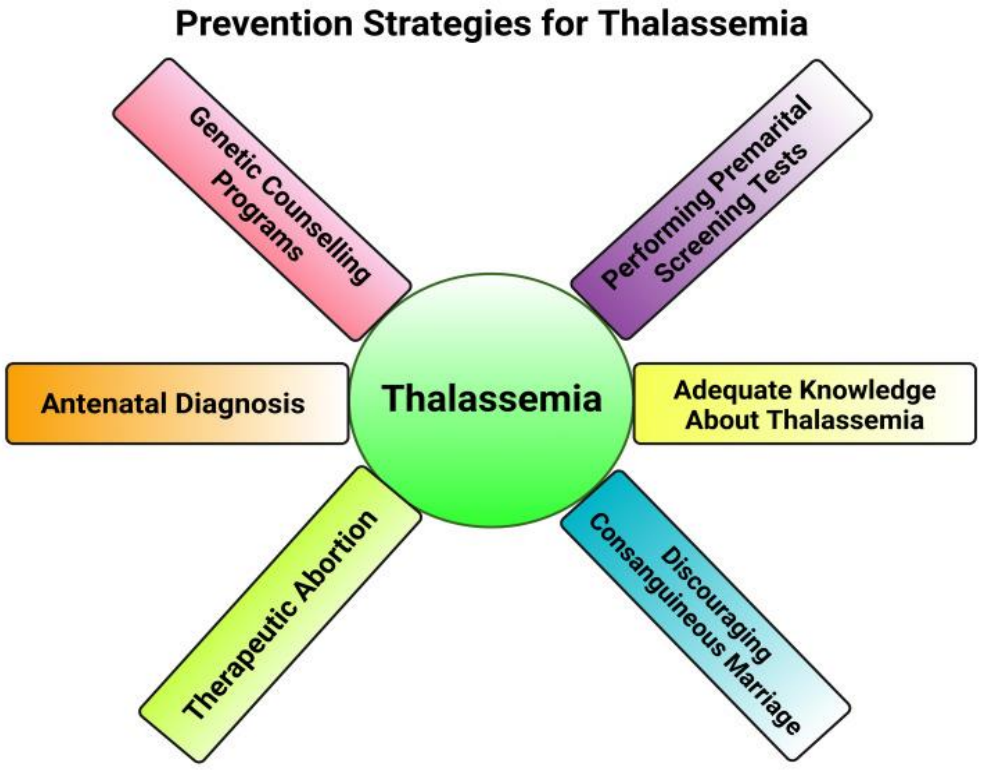

Figure 3: Prevention Strategies for Thalassemia

5.2 Management practice of thalassemia in Bangladesh

Standard management of thalassemia requires a multidisciplinary approach involving various specialties such as pediatric hematology, pediatrics, transfusion medicine, endocrinology, cardiology, dentistry, dietetics, psychology, psychiatry, social work, and a well-supported blood bank system [36]. However, in developing countries like Bangladesh, these specialized services and support systems are often unavailable in most public hospitals and private clinics. Additionally, health awareness among the general population in Bangladesh is very low, and there is no organized patient referral system. Consequently, many thalassemia patients may die without even knowing they have the disease due to inadequate access to healthcare. Furthermore, Bangladesh lacks a national policy or health insurance system for thalassemia prevention. To illustrate the current state of thalassemia management in Bangladesh, this article presents the experiences from the Thalassemia Foundation Hospital (TFH) [37].

Patient and clinical set up of TFH

Our study center is one of only two specialized hospitals in the country dedicated exclusively to treating thalassemia patients. Located in Dhaka, the capital of Bangladesh, TFH was established by a group of thalassemia supporters and families of patients. It began as a small discussion group focused on sharing updated information on thalassemia management and addressing the challenges faced by patients and their families. Over the next few years, the number of patients increased significantly [38]. The main issues highlighted by the families were the lack of iron chelator medicines and the need for a convenient transfusion facility. To tackle these issues, TFH commenced its operations in 2008, offering day-care services such as blood transfusions, expert consultations, medications, and laboratory tests from a single location. The hospital is currently managed by two senior hematologists, one transfusion medicine consultant, and a team of 15 doctors, nurses, and support staff [39]. This study included patients who attended TFH from January 2009 to December 2014. The hospital-based retrospective study received ethical approval from the Ethical Review Committee of Bangladesh University of Health Sciences (Memo No: BUHS/ERC/16/031). Patient charts were reviewed, and each patient was assigned a unique ID upon registration to maintain proper documentation. During the initial visit, a detailed history, physical examination findings, height, and weight were recorded. Tests

such as CBC, Hb electrophoresis (preferably at the time of diagnosis and prior to transfusion), basic metabolic panel, liver function tests, and baseline iron status were conducted [40]. Patients were assessed for transfusion requirements and monitored for four weeks, followed up for clinical symptoms and Hb levels. Stable patients after this period were further monitored to determine steady-state Hb and the correlation of Hb with clinical symptoms, allowing clinical categorization into thalassemia intermedia and determination of transfusion triggers. Follow-up visits every 4–6 weeks assessed quality of life (QOL), organomegaly progression, and growth failure. Transfusion-dependent patients were monitored for iron loading and medication side effects. Hydroxyurea was administered to thalassemia intermedia patients, with follow-ups for QOL and Hb increment [41]. Over the five-year period from 2009 to 2014, TFH served a total of 1,594 thalassemia patients, out of which 1,178 complete cases were analyzed, revealing a male-to-female ratio of 1.26. All thalassemia cases were diagnosed using conventional electrophoresis methods. Approximately 77.3% of patients were diagnosed with HbE beta thalassemia, while nearly 15% had beta thalassemia major. About 91% of patients (n = 971) required blood transfusions, with approximately 66.9% being transfusion-dependent thalassemia (TDT) patients and 24.3% being non-transfusion dependent thalassemia (NTDT) patients. Around 41.1% of TDT patients required blood transfusions every 2–4 weeks. Due to incomplete medical records, transfusion history was missing for 115 diagnosed cases (approximately 9.7% of all cases) [42].

Transfusion practice

Thalassemia carriers are generally healthy and do not need blood transfusions. Non-transfusion dependent thalassemias typically include HbE beta thalassemia and beta thalassemia intermedia, which do not require regular transfusions for survival. However, at TFH, some diagnosed carrier patients were admitted as transfusion-dependent thalassemia (TDT) cases (10 patients) and non-transfusion dependent thalassemia (NTDT) cases (17 patients) [43]. Factors like infection and iron deficiency, especially in women of reproductive age, can worsen pre-existing anemia, leading to unnecessary transfusions. This could stem from misdiagnosis or a lack of awareness among clinicians in Bangladesh. Thalassemia intermedia (TI) refers to patients with beta thalassemia who exhibit clinical

severity between transfusion-dependent thalassemia major and the milder beta thalassemia trait. Most TI patients are either homozygous or compound heterozygous for beta thalassemia. In Southeast Asia, including the Indian subcontinent, severe thalassemias often result from the coinheritance of HbE and beta trait. HbE beta thalassemia can be categorized based on clinical severity into mild (15% of cases), moderately severe (the majority), and severe, with up to 50% of HbE beta thalassemia patients showing symptoms similar to beta thalassemia major [44]. Managing NTDT is challenging due to its clinical diversity, relying mainly on clinical observations. In our study, over 62% of HbE beta thalassemia patients were treated as TDT, while about 28% were NTDT. The unexpectedly high proportion of transfusion-dependent HbE beta thalassemia in Bangladesh might result from misdiagnosis or using Hb levels alone to determine the need for transfusions, instead of other criteria like growth failure, delayed puberty, splenomegaly, thrombosis, and pulmonary hypertension. A complete mutation profile (DNA testing) before treatment can help determine prognosis, appropriate therapy, and family counseling. Increased clinician awareness is essential for proper NTDT diagnosis and management [45]. Studies have highlighted the limitations of using Hb levels alone for initiating transfusion-dependent management, as Hb levels only slightly differ between the mildest and most severe forms of HbE beta thalassemia. Some children with HbE beta thalassemia adapt to lower Hb levels and lead nearly normal lives without transfusions. A study in Sri Lanka found that about 42% of HbE beta thalassemia patients could switch from TDT to NTDT without adverse conditions, indicating many may have received unnecessary regular transfusions. NTDT patients might experience severe anemia due to acute infections, but regular transfusions are not recommended immediately after NTDT diagnosis. While transfusion therapy can benefit some patients if administered correctly, it should not be necessary for survival. In developing countries, transfusion-dependent families face challenges like pathophysiological, psychological, and financial burdens, and the regular arrangement of safe blood. In Bangladesh, 85% of blood is donated by patients' relatives and friends, with the remaining 15% from voluntary donors. Accurate diagnosis should be mandatory before starting transfusion therapy to ensure proper thalassemia management [46].

Infection

Patients with transfusion-dependent thalassemia (TDT) are at risk of contracting post-transfusion hepatitis, with hepatitis B and C being the most prevalent. The lack of effective vaccines for HCV and insufficient infection control measures make HCV a significant public health issue in low to middle-income countries. Globally, approximately 180.5 million people are infected with HCV, with 54.4 million of these cases in South Asia. Studies indicate that the prevalence of HCV among frequently transfused thalassemia patients ranges from 3% to 67.3% [47]. The heightened risk of HCV infection in β-thalassemia patients is primarily linked to factors such as median age, transfusion duration, and the average amount of blood transfused. No HIV cases were detected among transfusion-dependent patients. For HBV, 6 out of 523 tested cases were positive among those who had undergone blood transfusions. In the current study, 28.3% of the tested cases (n = 247) who had multiple transfusions were found to be HCV positive. Another study in Bangladesh also reported a high prevalence of HCV among multi-transfused thalassemia patients [48].

Iron chelation and hydroxyurea therapy

In our study, about 43% of the patients (n=972) receiving multiple blood transfusions were administered iron chelators to eliminate excess iron from their bodies. Deferiprone was the most frequently used iron chelator (n=481), followed by Deferasirox (n=199) and Desferal (n=91). Additionally, nearly 43% of the patients (n=972) who underwent regular or occasional transfusions received hydroxyurea therapy to boost fetal hemoglobin levels and reduce ineffective erythropoiesis [49].

Table 2: An overview of the treatment options for Thalassemia in Bangladesh

Treatment	Description	Availability in Bangladesh	Effectiveness	Reference
Blood Transfusions	Regular transfusions to maintain normal hemoglobin levels.	Widely available in major cities, limited in rural areas.	Effective in managing symptoms and preventing complications.	49
Iron Chelation Therapy	Medications (oral or injection) to remove excess iron from the body.	Available in specialized centers, less so in rural areas.	Essential for preventing iron overload due to frequent transfusions.	
Folic Acid Supplements	Daily supplements to help with the production of red blood cells.	Readily available across the country.	Supports overall health and red blood cell production.	50
Bone Marrow Transplant	Transplanting healthy bone marrow from a donor to replace the defective marrow.	Available in very few specialized hospitals.	Potentially curative but very expensive and risky.	
Gene Therapy	Experimental treatment involving the insertion of normal genes into the patient.	Not yet available; still in clinical trials worldwide.	Promising future treatment, but not currently an option.	51
Hydroxyurea	Medication that can increase fetal hemoglobin production.	Limited availability; some hospitals and clinics.	Can reduce the frequency of blood transfusions needed.	
Supportive Treatments	Treatments such as managing infections, nutritional support, and regular monitoring.	Widely available but varies in quality.	Important for maintaining overall health and managing complications.	44

5.3 Complications of thalassemia and related issues

The burden of thalassemia on patients arises from the disease's complications and the consequences of its treatment. Patients dependent on transfusions often experience iron overload, necessitating iron chelation therapy. Long-term care and management, ideally overseen by hematologists, are essential [50]. Allergenic hematopoietic stem cell transplantation (HSCT) is the best curative option for severe thalassemia cases, but it is

often impractical due to challenges such as lack of HLA-matched donors, limited resources and expertise, high costs, and the significant risk of mortality and morbidity associated with HSCT [1,21,22] (Figure 2) [51]. Recent advancements in blood transfusions and iron chelation therapy have led to a decreased mortality rate in Western countries, dropping from 12.7 deaths per 1000 patients between 1980-1999 to 1.65 deaths per 1000 patients from 1999-2013. Despite this, high morbidity rates persist in older patients due to long-term exposure to disease and treatment-related side effects, including transfusion and transplantation complications, hepatitis C, iron overload issues, bone disease, endocrine disorders, and other complications, as well as premature death [23,24]. Transfusion-dependent patients typically have a poorer health-related quality of life compared to non-thalassemia patients due to underlying issues such as splenectomy, stunted growth, malnutrition, and prolonged hospital stays [21]. They often experience feelings of hopelessness, low self-esteem, lower IQ, poor academic performance, and social isolation [25]. Both patients and their family members, especially mothers, endure significant physical, mental, and social distress [52].

Chapter 6
Conclusion

6. Conclusion

The review on the current status and treatment options for thalassemia in Bangladesh highlights a critical public health challenge that requires urgent and coordinated action. Despite advances in medical technology and treatment modalities, thalassemia continues to exert a significant burden on affected individuals and their families, primarily due to high prevalence rates and inadequate healthcare infrastructure. Effective management of thalassemia in Bangladesh necessitates a multi-faceted approach that includes enhancing public awareness, expanding carrier screening programs, and improving access to advanced treatments such as bone marrow transplantation and emerging gene therapies. Government initiatives, along with support from non-governmental organizations, are crucial in developing comprehensive care strategies and ensuring sustainable funding for thalassemia treatment centers. Educational campaigns to inform the public about the importance of early diagnosis and preventive measures, such as prenatal screening, can significantly reduce the incidence of severe cases. Additionally, investment in healthcare infrastructure, training of medical personnel, and research into new treatment options will be vital in addressing the challenges posed by thalassemia. In conclusion, while Bangladesh faces significant challenges in managing thalassemia, there is a path forward through strategic public health initiatives, improved medical care, and continued research. By implementing these measures, it is possible to enhance the quality of life for thalassemia patients and work towards reducing the prevalence and impact of this debilitating genetic disorder in the country.

Chapter 7
Reference

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