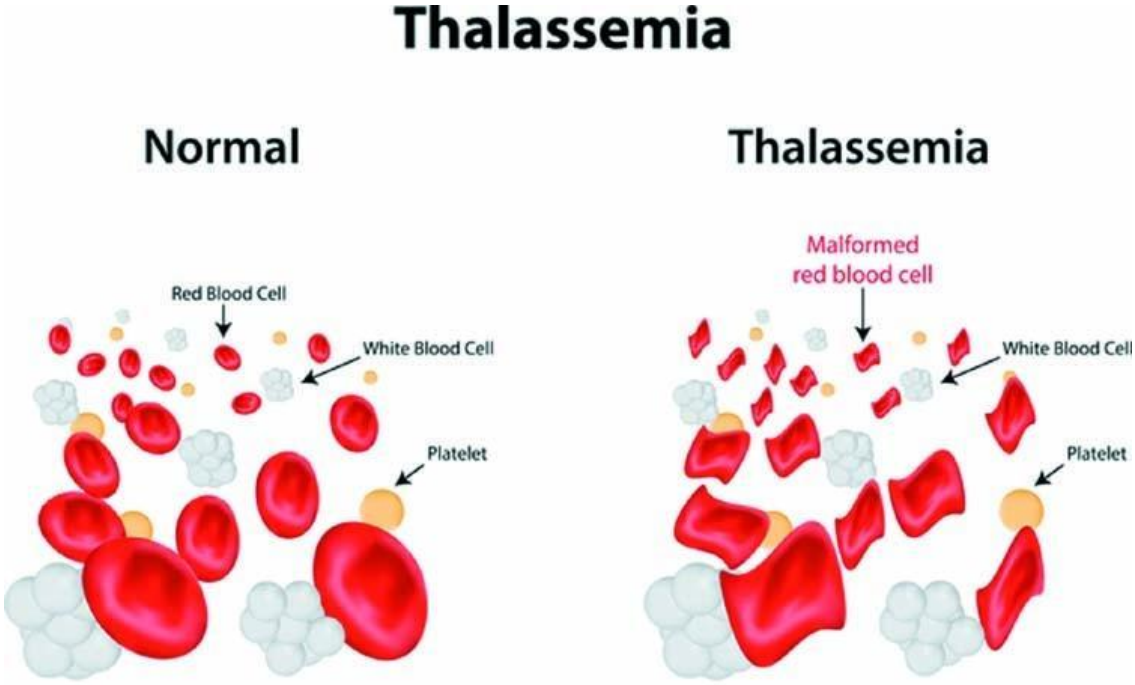
What is thalassemia?

Thalassemia is an inherited blood disorder that causes the body to produce less hemoglobin, the protein in red blood cells that helps them carry oxygen from the lungs to all parts of the body. Hemoglobin is made up of four parts: two alpha proteins and two beta proteins. Thalassemia affects one or more of the genes that produce these proteins.

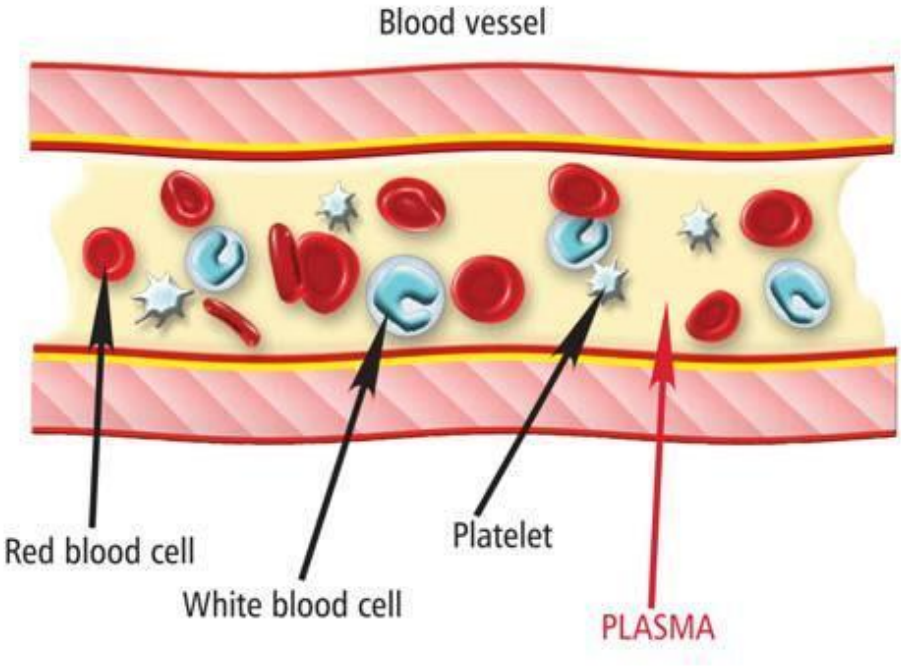


In shorts: About haemoglobinopathies

Haemoglobin disorders or haemoglobinopathies are a group of conditions affecting the human blood – more specifically an important substance or protein called haemoglobin contained in the red blood cells, hence the name haemoglobin disorders or haemoglobinopathies.

Haemoglobin is a protein that consists of the alpha (α) and beta (β) parts or chains and which are in turn produced by the α-globin genes and β-globin genes respectively. Hence the diseases caused by haemoglobin abnormality either with regards to its production or its structure are divided into α-chain diseases (or α-globin gene) diseases, such as α-thalassaemia, and β-chain (β-globin gene) diseases, such as β-thalassaemia major and sickle cell disease.

These genes are found on chromosomes 16 and 11 respectively, producing equal amounts of α and β chains respectively which match together to α2β2 to produce the normal adult haemoglobin (HbA, α2β2).



The severity of the disease depends on the type of thalassemia. Children with thalassemia major require ongoing treatment and blood transfusions throughout their lives. In addition, they need ongoing chelation therapy to remove the excess iron that builds up in the blood from these transfusions. Milder forms of thalassemia, including thalassemia intermedia and thalassemia minor, require less aggressive or no treatment at all.

Everyone has four alpha genes and two beta genes that together control the production of hemoglobin. There are three major types of thalassemia, classified based on the severity of symptoms and the genetic defect causing the disease.

What are the types of thalassemia?

Thalassemia minor and silent carriers

Children with thalassemia minor or trait have two alpha genes or one beta gene missing or damaged, while those that are “silent carriers” have one missing or

damaged alpha gene. These children do not experience symptoms (except mild anemia in some cases of thalassemia minor), and they do not require treatment.

Thalassemia intermedia

In children with beta thalassemia intermedia, one or both beta genes are not working properly. They have mild to severe anemia andcan be diagnosed early in childhood or later in life. They may need blood transfusions during pregnancy or when very sick.

Thalassemia major

Children with thalassemia major need ongoing medical care, including blood transfusions to alleviate severe anemia and chelation therapy to remove excess iron from the blood. There are two subtypes of thalassemia major:

Alpha thalassemia major

- most serious and most rare form of the subtypes of thalassemia
- all four alpha genes are missing
- if untreated, leads to miscarriage or death of the baby shortly after birth
- may be treated with blood transfusions in the womb if discovered early enough in the pregnancy
- babies who survive require lifelong blood transfusions or stem cell transplant and extensive medical care

Beta thalassemia major (also called Cooley's anemia, after the discoverer)

- neither beta gene is not working properly
- symptoms, which begin during the first year of life, include severe anemia
- monthly blood transfusions needed
- chelation therapy also is needed to remove excess iron that builds up in the body due to frequent blood transfusions

Other types of thalassemia

Hemoglobin E beta-thalassemia: This form of thalassemia is more common in children of Southeast Asian descent. It results from two separate genetic defects:

Hemoglobin H disease alpha-thalassemia: This form of thalassemia is most common in Southern China and Southeast Asia. In Hemoglobin H disease:

The defective genes that cause thalassemia are relatively common, especially in people of South Asian, African and Mediterranean descent. However, thalassemia occurs in many populations around the world.

Haemoglobin disorders, including thalassaemia are an international concern. It is estimated that 7% of the world population is a carrier of a severe haemoglobin disorder and 300-500.000 children are born with a severe haemoglobin disorder each year. Research advances in the clinical care of thalassaemia have managed to transform thalassaemia from a fatal disease of childhood that it once was into a chronic, yet well-managed disease, increasing patients' survival rate and improving their quality of life.

Bangladesh is a high prevalence country in consideration of Haemoglobin disorders. It is considered that among its 170 million people 4.1% (range 1-5%) are carriers of beta Thalassaemia, a non communicable disease, while 6.1% (range 4-10%) are carriers of the variant HbE. This means that an estimated 14500 new births of affected children are expected every year. A current estimate is that there may be up to 90000 patients with clinically significant Haemoglobin disorders living in the country at any time. The purpose of the study is to know about the Thalassaemia burden in Bangladesh and to develop a tool to diagnose Thalassaemia based on patients economic characteristics.

Hemoglobin E disease and hemoglobin E/beta thalassemia are extremely common in Southern China, and South and Southeast Asia.

Prevalence of Thalassaemia:

The prevalence rate of haemoglobinopathies in Bangladesh is not well documented. A study on Bangladeshis living in UK is cited as a document by WHO. WHO data shows carrier status of Beta Thalassaemia trait to be 3% & Hb E trait to be 4%. However, much of the data available from WHO was based on studies that were carried many years ago and no regional data are available and there is no data base also.

In 2003 the Bangladesh Thalassaemia Samity could get some fund from Canadian International Agency (CIDA) to upgrade the facilities of the hospital. Part of the fund was allowed by CIDA to conduct a survey. Thus, with this fund a total number of 1248 samples of blood were collected from high school and college students during the last 6 months of 2003. More that 50% of the samplelwere from girls.The result from the study showed that average Hb E trait 5.17% and Beta Thalassaemia trait 4.20% in Bangladesh. Moreover Regional data showed that in Dhaka division Hb E 4.27%, Beta Carrier 3.61%, Chittagong division Hb E trait 6.42%, Beta Carrier 5.52%, Rajshahi division Hb E trait 8.69%, Beta Carrier 12% Khulna division Hb E trait 8.53%, Beta Carrier 4.87% ,Barisal division Hb E trait 2.9%, Beta Carrier 0, Sylhet division Hb E trait 0 & Beta Carrier 6.67% .Another study was done by Dr. Waqar Ahmed khan& others to determine the prevalence of Beta Thalassaemia trait and Hb E trait in school children of Bangladesh and calculate the health burden of Thakassaemia.Haemoglobin Electrophoresis was done on blood collected from 735 school children from all six divisions of Bangladesh.

Over all prevalence of Beta Thalassaemia trait was 4.1% and Hb E trait was 6.1% in Bengali school children. The prevalence of Beta Thalassaemia trait in Bengali school children in Barisal division was 8.1% which was the highest followed by Rajshahi division 5.5%, Sylhet division 5.2%, Dhaka division 3.2%, Chittagong 2.9% & khulna division 2.4%. In tribal school children of Chittagong the prevalence rate of beta trait was 4.2%. Prevalence of Hb Etrait was 16.5% in Rajshahi division which was highest in Bengali school children followed by Barisal with prevalence of 8.1%, Dhaka 8%, Sylhet 4.2%, Chittagong 2.9% and khulna 2.4%. Prevalence of Hb E was 41.7% in tribal school children and 4.2 % were beta-thalassaemia carrier.

Recent epidemiological data published by TIF shows that Bangladesh is one of the most highly affected country with heamoglobin disorder in Asia with the carrier and frequency rates

a) Thalassaemia Trait – 4.1 %
b) Heamoglobin E trait – 6.1 %
c) Anticipated new affected births annually: 6435 based on carrier rate, population size and other demographic indicies.
d) Living patient with thalassaemia – 50,000 to 60,000.

In recent study of Bangladesh Thalassaemia Samity Hospital, was carried out among student volunteers mainly in Dhaka and once in Noakhali and once in Bogra. The districts of origin of all the volunteers were recorded while taking blood samples. The test results of 1439 samples were put in a database, these were analysed and following are the findings.

The Division Wise Distribution of Persons with Thalassaemia Traits

The number of volunteers tested division wise is given in below. The number of volunteers is maximal in Dhaka, Rajshahi and Chittagong as samples were collected in these divisions only. The test results did not only identify trait carrier but small number of Hb E diseased persons. All critical and major complications among patients take place in the childhood. Hb E is not a major problem but may be in danger at some situations like delivery etc.

Division wise Distribution of Thalassaemia Carriers

Name of Division	Number of Persons Tested to be Normal or Bearers				
	Number tested	Non Thalassaemia	Hb E Trait	β Thalassaemia traits	Haemoglobinopathy Diseased
Barisal	77	69	4	2	2
Chittagong	260	227	21	9	1
Dhaka	475	420	39	12	4
Khulna	159	149	8	2	0
Rajshahi	338	280	51	8	4
Rangpur	116	73	31	5	7
Sylhet	14	12	1	1	0
Total	1439	1230	155	39	18

Tests carried out on persons aged between 12 – 40 years; however most of persons were within the age 20- 27 years. The test depicted the following features. In the country about 14.0% healthy looking young people are carriers of Thalassaemia trait and 1.3% of persons are Hb-E diseased. Figure 5.2 beside shows that the prevalence of Hb-e is as high as 10.8 %. The occurrence of β Thalassaemia is 2.7%. The situation is not uniform through the country. The variation inside each division is described in the following sections.

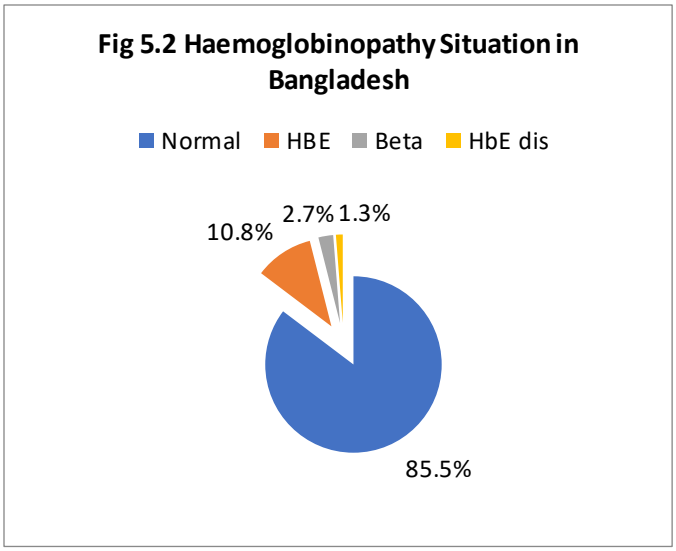
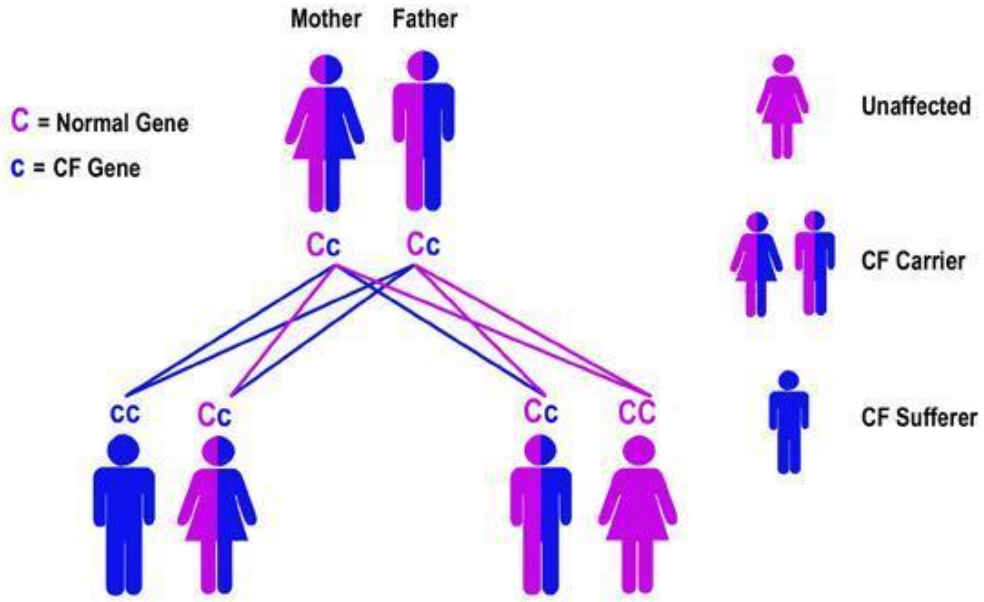


Fig 5.2 Haemoglobinopathy Situation in Bangladesh

What causes thalassemia?

Thalassemia is caused by an abnormality or mutation in the DNA of the cells involved in hemoglobin production. Children inherit this condition from their parents. When one parents is a carrier for thalassemia, a child may develop a form of the condition called thalassemia minor. When both parents are carriers of thalassemia, there is a greater chance their child or children will inherit a more serious form of the condition.



What are the symptoms of thalassemia?

Symptoms of thalassemia depend on the clinical severity of the disease and the therapies employed to treat it. Each child may experience symptoms differently. Patients with thalassemia trait generally do not experience any symptoms.

Transfusion dependent thalassemia

The primary signs and symptoms of Thalassaemia Major in infancy, before diagnosis, are those of,

- Severe anemia
- Hepatomegaly
- Abdominal Pain
- Jaundice
- Splenomegaly
- Bony Change
- Development Dely
- Facial Disfigurement
- Swollen Abdomen

- Failure of Thrive

Later in childhood and adulthood, transfusion dependent thalassemia symptoms are generally the result of iron overload, a byproduct of the frequent blood transfusions patients with this form of thalassemia require.

Patients with transfusion dependent thalassemia do not typically experience severe anemia once they have started receiving regular transfusion. Without these transfusions, however, they can develop life-threatening anemia.

Symptoms of iron overload may include:

- Chronic fatigue
- liver disease
- abdominal pain
- heart problems
- joint pain

Non-transfusion dependent thalassemia

The most common symptoms of non-transfusion dependent thalassemia are related to anemia:

- pale skin, lips, hands or under the eyelids
- increased heart rate (tachycardia)
- breathlessness, or difficulty catching a breath (dyspnea)
- lack of energy, or tiring easily (fatigue)
- dizziness or vertigo, especially upon standing
- headache
- irritability
- irregular menstruation cycles
- absent or delayed menstruation (amenorrhea)
- slow or delayed growth and development
- bony overgrowth or deformities
- an increased risk of bone fractures

How we care for thalassemia

The treatment of thalassemia is regular blood transfusion at 2-4 week intervals to correct the anemia. A safe and sustainable supply of blood is needed to cater the thalassemia patients. Ideally, the patients need leuko-reduced (free of white blood cells) red blood cell. Alternatively, a bedside leukoreduction filter is used to reduce the white cells from blood. A significant number of patients contract transfusion-transmitted infection such as Hepatitis B and C.

Chronic blood transfusion results in toxic iron accumulation in vital organs of the patient such as liver, heart, and pancreas. The iron overload gives rise to further complications such as heart failure, liver cirrhosis, diabetes, and growth retardation. Consequently, the patients have to take iron reducing medications throughout their lives to mitigate the iron toxicity. The currently available medications are desferrioxamine, deferiprone, and deferasirox. Desferrioxamine is available only in injectable form and must be taken subcutaneously with a portable infusion pump over 8-12 hours for 5 days/week.

The only cure for thalassemia is bone marrow transplantation (BMT). But its potential widespread application is limited by several factors. Firstly, BMT for thalassemia requires a matched sibling donor. Such donor is available in only 1-2% families. Secondly, there is a significant mortality and rejection risk associated with BMT compared to conventional treatment with blood transfusion. It is also an expensive procedure and most families cannot afford it.