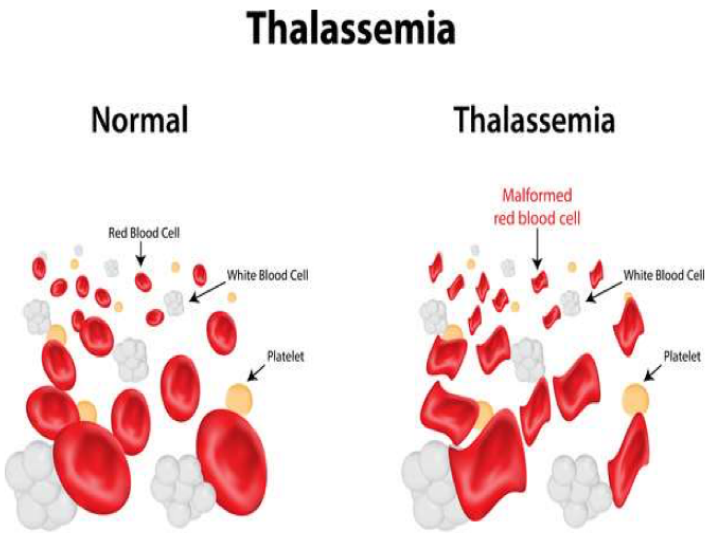
Thalassemia

Thalassemia is an inherited blood disorder in which the body produces an abnormal form of hemoglobin (Hb) which represents a protein molecule in red blood cells that carries oxygen. It is a group of diseases that have an autosomal recessive genetic basis involving inadequate production of normal Hb. Hb level in this genetic disorder is lower than normal, causing a decrease in blood oxygen level. The disorder results excessive destruction of red blood cells, which leads to anemia. Anemia is a condition in which your body doesn't have enough normal, healthy red blood cells. This disease is also called Mediterranean anemia, because the disease originated in the Mediterranean basin.



Incidence of Thalassemia

Thalassemia is commonly found in members of ethnic groups whose origins are near the Mediterranean Sea and equatorial or near - equatorial regions of Asia; the Middle East, and Africa. It represents a commonest group of autosomal recessive disorders in India. Carrier frequencies vary from 3% to 17% in different populations, with over 30 million people carrying the defective gene. About more than 9000 thalassemic children are born every year in country.

The causes of Thalassemia

Thalassemia occurs when there's an abnormality or mutation in one of the genes involved in hemoglobin production. Hb is made up of two proteins: – Alpha globin and Beta globin. Thalassemia occurs when there is a defect in a gene that helps in control production of one of these proteins.

Thalassemia is inherited, meaning that at least one of your parents must be a carrier of the disorder. If only one of your parents is a carrier for thalassemia, you may develop a form of the disease known as thalassemia minor. If both of your parents are carriers of thalassemia, you have a greater chance of inheriting a more serious form of the disease.

Types of Thalassemia

The types of thalassemia depend on the following: The affected part of hemoglobin (alpha or beta) and severity of disease. There are three main types of thalassemia (and four subtypes):

- Alpha thalassemia, which include the subtypes hemoglobin H and hydrops fetalis
- Beta thalassemia, which includes the subtypes major and intermedia
- Thalassemia minor which is less serious for of this disorder.

All of these types and subtypes vary in symptoms and severity. The onset may also vary slightly.

A) Alpha thalassemia:

It is a form of thalassemia involving the genes HBA1 and HBA2. Hemoglobin consists of four genetic chains of alpha type, two from the father and two from the mother. It results when there is disturbance in production of α-globin from any or all four of the α- globin genes. It is most commonly seen in people of Asian and African descent. The α-globin genes are encoded on chromosome 16.

In a normal cell, the α-globin chains are coded by a total of four alleles. Thus, there are four forms of the disease. The severity of alpha thalassemia depends on the number of defective α-globin alleles.

1. **Silent carrier (minima form):**

This is known as alpha thalassemia silent and with this type, the effect on hemoglobin synthesis is minimal because there is only one defective allele (-α/αα). However, three α-globin genes are enough to permit normal hemoglobin production, and no clinical symptoms present (asymptomatic). It occurs due to a deletion or non-deletion mutation.

2. **Alpha thalassemia trait (minor form):**

In this type, there are two defective alleles (-α/-α or --/αα). Two α genes permit nearly normal production of red blood cells, but a mild microcytic hypochromic anemia is seen. The disease in this form can be mistaken for iron-deficiency anemia and treated inappropriately with iron. Alpha-thalassemia trait can exist in two forms:

- **Alpha-thal-1** (- -/α α), involves cis deletion of both alpha genes on the same chromosome. Higher incidence in people of Asian descent when compared with the general population.
- **Alpha-thal-2** (- α/- α), involves trans deletion of alpha genes; this occurs on different (homologous) chromosomes. Higher incidence in people of African descent when compared with the general population.

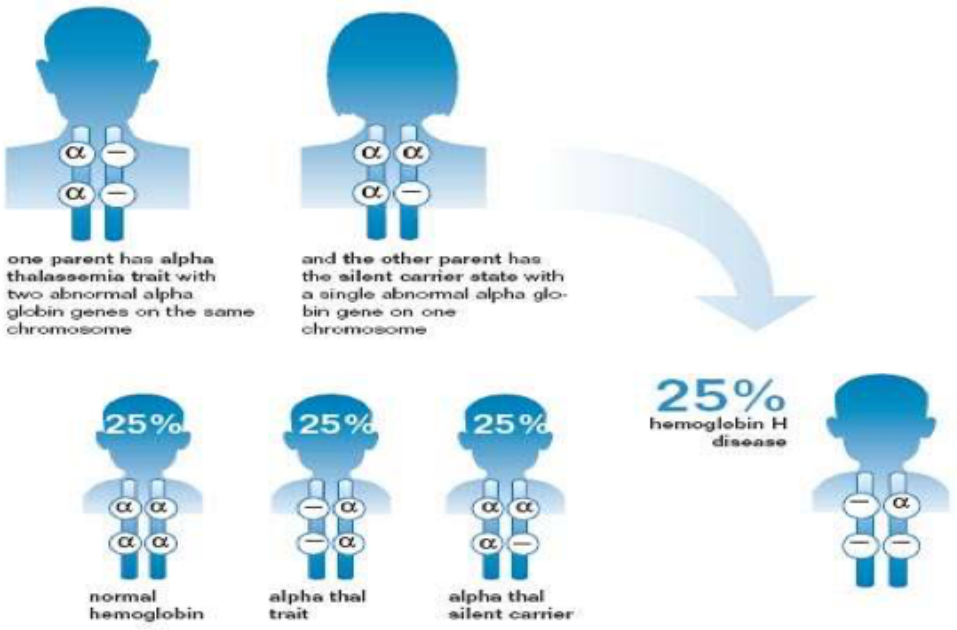
3. **Hemoglobin H disease (intermedia form):**

Three defective alleles (--/-α) results in excessive production of pathologically altered HbH. Two unstable hemoglobins are present in the blood; hemoglobin Barts (tetrameric γ chains) and hemoglobin H (tetrameric β chains). Both of these unstable hemoglobins have a higher affinity for oxygen than normal hemoglobin. The patient would have Jaundice and severe anemia, symptoms vary between moderate and severe, and may develop hepatosplenomegaly and bone deformity. Compared to thalassemia beta, symptoms in adults are generally less severe.

4. **Hemoglobin Bart disease (major form):**

This is known as alpha thalassemia major; these fetuses are edematous, have little circulating hemoglobin, and the hemoglobin that is present is all tetrameric γ chains.

When all four alleles are affected (--/-), the fetus likely will not survive gestation without in utero intervention; most infants with alpha-thalassemia major are stillborn with hydrops fetalis.



B) Beta thalassemia:

Beta thalassemias are a group of inherited blood disorders. They are forms of thalassemia caused by reduced or absent synthesis of the beta chains of hemoglobin that result in variable outcomes ranging from severe anemia to clinically asymptomatic individuals. Beta thalassemias occur due to malfunctions in the hemoglobin subunit beta or HBB. The severity of the disease depends on the nature of the mutation.

Three main forms have been described: thalassemia major, thalassemia intermedia, and thalassemia minor.

1. **Beta thalassemia minor (trait):**

There is only one β globin defective allele. Individuals will suffer from microcytic anemia. Detection usually involves lower than normal mean corpuscular volume value (<80 fL). The patient needs blood transfusion to be able to live normally.

2. **Thalassemia intermedia:**

It is a form of Thalassemia which is characterized by mild to moderate anemia. Affected individuals can often manage a normal life but may need occasional transfusions, e.g., at times of illness or pregnancy, depending on the severity of their anemia.

3. **Beta thalassemia major (Cooley anemia):**

Occurs when both alleles have thalassemia mutations. This is a severe microcytic, hypochromic anemia. The patient suffers from severe anemia, bone deformity and spleen enlargement, and needs regular blood transfusions to survive normally. These symptoms do not appear when the baby is born; But begin to appear during the first two years of life.