# THALASSEMIA

Thalassemia is an inherited blood disorder that results from reduced production of hemoglobin, a protein present in red blood cells responsible for carrying oxygen throughout the body. . A hemoglobin molecule has two subunits, commonly referred to as Alpha and Beta. The gene locus controlling the production of alpha chains is called the alpha globin gene cluster, and similarly the beta globin gene cluster produces beta chains. A lack of a subunit determines the type of the resulting thalassemia (alpha or beta). Alpha and beta thalassemia are the most common inherited single-gene disorders in the world, with the highest prevalence in areas where malaria was or is still endemic (Mediterranean Basin, Australasia, the Americas, and Africa). In many parts of the world, thalassemia still represents a major public health concern.

In alpha-thalassemia, mutations in alpha-globin genes can give rise to a range of clinical presentations. The loss of one gene slightly diminishes the production of the alpha chain. The loss of two genes produces a condition with small red blood cells, and at most a mild anemia. Either of these conditions is not life-threatening and do not show any major symptoms. The loss of three alpha genes results in HbH disease characterized by anemia, liver and spleen enlargement, mild jaundice, and at times bone deformities. The loss of all four alpha genes causes Hemoglobin Barts Hydrops Fetalis, a condition that leads to fetal death.

In beta-thalassemia, symptoms occur starting from 6 to 24 months of age. The severity of the condition depends on the type of mutation. Some mutations (beta-zero) prevent any formation of beta chains; others (beta-plus) allow some beta chain formation to occur. In the most severe form of the disease, the bone marrow expands as it tries to compensate for the perceived need of new red blood cells, which could cause moderate to severe skeletal deformities and pain. Without proper treatment, the affected infants fail to thrive and become progressively pale. Feeding problems, diarrhea, irritability, recurrent bouts of fever, leg ulcers, osteoporosis, thrombotic complications, and progressive expansion of the abdomen caused by liver and spleen enlargement may occur.

## RISK FACTORS

People with Mediterranean (including North African), Middle Eastern, or Southeast Asian ancestry are at higher risk of being carriers of alpha or beta thalassemia.

Beta-thalassemia develops when the affected individual inherits two defective beta-globin genes from the parents. If only one defective copy of the beta-globin gene is inherited, mild symptoms may appear in some cases; this condition is called beta-thalassemia minor or beta-thalassemia trait. The inheritance of alpha thalassemia, however, is more complex because of the involvement of 1 to 4 copies of alpha globin genes. A positive family history of alpha or beta thalassemia is an important indication for an individual to seek consultation as he/she might be at high risk of carrying the disease.

## DIAGNOSIS AND MANAGEMENT

Diagnosis of thalassemia can be made as early as 9-11 weeks of pregnancy using procedures such as chorionic villi sampling. Analyzing the amniotic fluid may be carried out at 16-20 weeks of pregnancy. Individuals can also be tested for thalassemia through routine blood counts.

Early treatment of beta-thalassemia has proved to be very effective in improving the quality of life of patients. Long term transfusion support is the conservative approach for beta thalassemia patients to alleviate anemia. Frequent blood transfusions usually lead to iron overload that is countered through iron chelation therapy to prevent damage to the internal organs. In recent years, bone marrow transplantation has shown promise in many patients, where a successful transplant can eliminate their dependency on blood transfusions.

Untreated beta thalassemia eventually leads to death usually by heart failure. Therefore, genetic testing, counselling, and prenatal diagnosis are very important in the prevention, management, and treatment of this disease. In some Mediterranean countries, such as Cyprus, established control programs have achieved higher prevention rates (over 80%) in newborns.

## THALASSEMIA IN THE ARAB WORLD

Alpha and beta thalassemia are endemic in almost all Arab countries probably due to the historical presence of malaria in the region and high levels of consanguinity. Studies show high prevalence rate of alpha thalassemia in Oman (39%), Bahrain (24%), Saudi Arabia (16.3% - 28%) and the UAE (16.5%). However, it is possible that the prevalence rate for alpha thalassemia in the UAE might be even higher as a recent study indicated that the carrier rate may be around 49%. Countries in the region with relatively lower frequencies of alpha thalassemia include Qatar (3.2%) and Kuwait (4.6%). Comparatively, beta thalassemia prevalence data is limited, and available sources indicate lower rates ranging from 1.5% to 8.5%.

The molecular basis of beta thalassemia has been extensively studied in various Arab countries. A total of over 60 mutations in the beta globin gene have been reported in Arab patients with beta thalassemia. A recent genetic study in Dubai demonstrated the presence of 51 mutations in the UAE population. As expected, each Arab country has its own characteristic spectrum of mutations. While some mutations appear in most countries, others seem to be regionally restricted paving the way to studies on their historical origins.

Extensive efforts have been taken to reduce the rates of thalassemia in Arab populations. Screening of newborns, children, and obligatory screening of couples before their marriage have been found to be very effective. In Palestine, for instance, adoption of obligatory screening of couples for beta thalassemia before the issue of a marriage certificate has decreased the number of marriages of carrier couples, which in turn has led to a reduction in the birth of children with this disease. In Dubai, premarital screening program has been very successful, driving dramatic reduction of babies born with beta thalassemia major.