Thalassemia Syndromes

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Thalassemia syndromes•

Definition: The thalassemia syndromes are syndromes that result from inherited abnormalities in globin synthesis that lead to decrease in the production of hemoglobin .Hemoglobin synthesis is depend on a balanced production of heme and globin chains; a decrease of one component will lead to a decrease in hemoglobin and hypochromic microcytic anemia

Composition of hemoglobin•

1-**Globin chains:** Hemoglobin is composed from two pairs of two types of globin chains:

a-Alpha (α) chains.

b-Non (α) chains.

2-**Fetal haemoglobin (HbF)**

a-Early in embryonic development, tow chains (the theta (θ) and zeta (ζ) chains are produced and combine with a beta (β) –like chain the epsilon (ε) chain to from hemoglobin (Gower1,Gower11 and Portland hemoglobins). The β chain is the component that predominates in adult hemoglobin .

b-Later in the first trimester, α chains combine with other β-like chains gamma (γ) chain to form HbF.

3-Adult hemoglobin:

a- Hemoglobin A (HbA) is the major component of adult hemoglobin and is composed of pairs of α chains and β chains. The β chains are synthesized early in the individual's development but do not predominant until the third month after birth.

b-Hemoglobin A2 (HbA2) is the minor component of hemoglobin (accounting for 2.5%) and composed of pairs of α chins and delta (δ) chains .

Pathophysiology of the thalassemias

a- **α thalassemia:** gene deletions are responsible for the decrease in or absence of α chain in most α thalassemia. In some forms of α thalassemia, such as hemoglobin H (HbH) disease the gene is detected. The defect in this situation is presumed to occur without a deletion.

b- **β Thalassemia:** in contrast to α thalassemia β thalassemia is usually due to an mRNA abnormality.

Classification of B thalassemia•

1- **β Thalassemia major (β° β°):** is the most sever β thalassemia and usually becomes apparent 3-6 months after birth when the switch from HbF to HbA takes place . The symbol β° indicates that there is a total absence of β chain production: α, γ, δ, or ε chain replaces it in one or both position

2-**β Thalassemia intermediate (β° β° or $\beta^{+}\beta^{+}$):** presents with abnormalities similar to those of β thalassemia major however the patient suffers only a moderate degree of anemia and has only an intermediate or no requirement for transfusion. These patients have chronic disease up to adult life. The symbol β^{+} indicates that there is a partial deficiency of β chain production.

3-**Hb lepore disease**: is an unusual type of thalassemia that occurs when fusion variations of α and β chains produce an abnormal hemoglobin

4- β Thalassemia trait (β β^{o} or β β^{+}): is relatively mild disease with few or no symptoms the diagnosis is made only upon conducting family study.

5-- β Thalassemia minor: can be detected only by genetic studies.

6- Hereditary persistence of fetal hemoglobin (HPFHb): is clinically different from, although related to β thalassemia in that β and δ-chain production are decreased .production of the adjacent γ-chain is enhanced , however ,and ,there for the synthesis of globin chains is more in balance than in **β** thalassemia .Anemia is mild or absent since there is no accumulation of a chains in the red cells .HPFH is characterized by the production of fetal hemoglobin in to adulthood

Diagnosis of β thalassemia•

a-Nonspecific findings:

1-Blood smear reveals microcytic red cells with poikilocytosis and fragmented dacrocytes .The MCV is low around 65fl.

2-Heinz bodies are evident by supravital staining with crystal violet.

1-Finding of β thalassemia:

a-Increased proportion of HbA2 (3.5%) normal is (2-3%).

b- Increased proportion of HbF in HPFHb (to70-100%) normal is (2-3%).

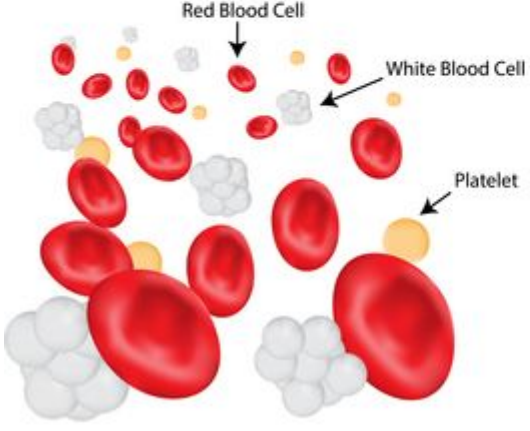
- **2-Differentiating features among β thalassemi**a

a- Decreased proportion of HbA in **β** thalassemia trait. b- Very little HbA in **β** thalassemia major.

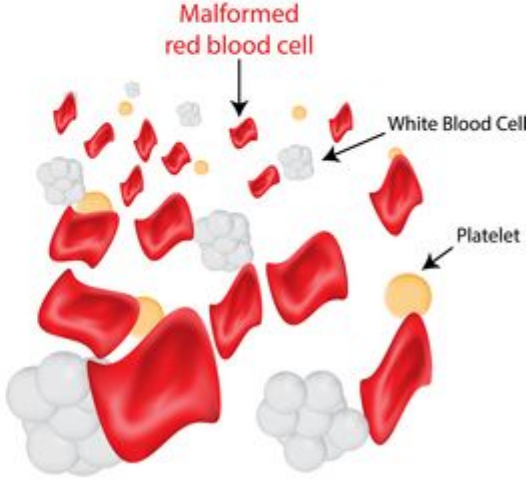
c- Absence of HbA2 in β thalassemia minor HPFHb and Hb lepore.

Thalassemia

Normal



Thalassemia



α thalassemia

In **α** thalassemia a decreased synthesis of **α** chains leading to the precipitation of HbH (abnormal hemoglobin composed of four **β** chains) or **Bart's** hemoglobin (an abnormal hemoglobin composed of four **γ** chains) results from genetic defects that prevent the formation of some or all of the necessary **α** globin.

Classification of α thalassemia

1-**Hydrops fetalis**: is the most severing form of α thalassemia all four α genes are deleted resulting in a severely anemic the **Bart's** hemoglobin causes morbidity and mortality in the infants because of its very high oxygen affinity.

2-**HbH disease:** Which is clinically similar to **β** thalassemia major is the result of three α genes deletion. Because of its instability HbH precipitates and result in extra vascular hemolysis.

3-**α thalassemia trait**: is the result of the deletion of two **α** gene the condition occurs in the offspring of two carrier parents or of an HbH parent and normal parent and is clinically similar to **β thalassemia minor.**

4- **α thalassemia carrier:** is the result of the deletion of one **α** gene these individuals are asymptomatic

Diagnosis of α thalassemia

a- Non specific findings:

1- Blood smears reveals microcytic hypochromic red cells target cells and anisopoikilocytosis. The MCV is low.

2- Heinz bodies are evident.

b- Specific findings: The definitive diagnosis of **α** thalassemia is based on the identification of HbH by hemoglobin electrophoreses