



Thalassemia

It is an **inherited** blood disorder effect on body ability to produce normal hemoglobin and healthy red blood cells, types include alpha and beta thalassemia. Thalassemia may cause anemia-like symptoms that range from mild to severe. Treatment can consist of blood transfusions and iron chelation therapy.

Thalassemia causes:

Any defective or missing in genes coding for globin chains in hemoglobin (Hemoglobin consists of four protein chains, two alpha globin chains and two beta globin chains) **are caused thalassemia.**

***Alpha globin protein chains consist of four genes**, two from each parent.

***Beta globin protein chains consist of two genes**, one from each parent.

The extent of the defect will determine disease severity.

Types of thalassemia:

There are **two types** of thalassemia — **alpha** and **beta** thalassemia — named after defects in these chains.

Each type of thalassemia is classified as **minor and major**. Thalassemia major is the most serious form and usually requires regular treatment, thalassemia minor means that you may experience mild anemia symptoms or no symptoms at all. You may not need treatment.

Alpha thalassemia types include deletion one, two, three and four genes deletion



Case 1	- α/α β/β	Silent carrier	Absent 1 alpha chain	Heterozygous
Case 2-1	- $\alpha/-\alpha$ β/β	Minor alfa thalassemia	Absent 2 alpha chains	Homozygous
Case 2-2	- $-\alpha\alpha$ β/β	Minor alfa thalassemia	Absent 2 alpha chains	Heterozygous
Case 3	- $-\alpha$ β/β	HbH	Absent 3 alpha chains	Homozygous
Case 4	- $-\alpha$ β/β	Barts hydrops fetalis	Absent 4 alpha chains	Homozygous

Table 1 alpha thalassemia types

A-The absence of 3 a-chains affect called HbH disease, started in fetus life and survive to adult life with (symptoms):

- 1- Severe anemia with hemolysis.
- 2- Occasionally blood transfusions are required
- 3- Severe RBC abnormalities
- 4- The absent of 3 alpha chains make Precipitated Hgb H inside the RBC

HbH disease diagnosed early at about **6 months**.

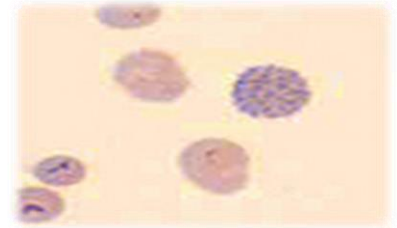
Laboratory diagnosis of HbH Thalassemia:

1-CBC		2-Blood film: ❖ Hypochromia (++ - +++) ❖ Microcytosis (++ - +++) ❖ Target Cells, Basophilic Stippling, Tear-Drops	3-HbH electrophoresis, the result may be as follow:	
Hb	Low		HbA	Absent
MCV	Low		HbA2	Normal
RDW	Normal		HbF	Slight elevated
Retic-count	Increase		*HbH	90%

Table 2 HbH diagnosis

Final Diagnostic tests:

1. Hb electrophoresis result indicate presence new Hb called HbH
2. DNA analysis searching for the alpha genes on the chromosome 16 (three are absent)
3. Red cell inclusion bodies in reticulocyte preparations (may be reach to 70% of all RBC) by supravital stain, increasing incubation time to cause precipitation giving the appearance of a **golf ball**



Hb inclusion inside RBC (golf ball)

B- Bart's hydrops syndrome occurs when no chains are made (deletion 4 chains), even in the fetus; these infants are usually stillborn at between 28 and 40 weeks, and if born alive, they die within the first hour.

Beta Thalassemia include **minor** type when mutation caused deletion of one beta chain, **and major** β –Thalassemia called (**Cooley's Anemia**) that defect in both beta chains (the tow beta chains are absent).

Homozygous	Major Beta thalassemia (Cooley's anaemia)	Absent 2 beta chains	aa/aa b ⁰ /b ⁰	Case 1
Heterozygous	Minor Beta thalassemia	Absent 1 beta chains	aa/aa b/b ⁰	Case 2
⁰ : Indicates no production of globin chain by gene ⁺ : Indicates diminished, but some production of globin chain by gene: defects in production of Hb β that leads to microcytosis				

Table 3 Beta thalassemia types

Symptoms of Cooley's Anemia:

- 1- Severe anemia at 6 months of birth.
- 2- HbF not developed to HbA in the first year of the life



- 3- The result remain the HbF all life with **sever hemolysis**
- 4-Most patients need regular transfusion.
- 5-The main problem of those patients is **iron loading**.

Laboratory diagnosis of Cooley's Anemia:

1-CBC		2-Blood film:	3-HbH electrophoresis, the result may be as follow:	
Hb	2-5g/dl	Hypochromia (++ - +++) Microcytosis (++ - +++) Target Cells, Basophilic Stippling, Tear-Drops Heinz Bodies Nucleated RBC +++ (bone marrow response)	HbA	Absent
MCV	Low		HbA2	Normal
RDW	Normal		HbF	Slight elevated
Retic-count	>15%		*HbF	90%

Table 4 laboratory findings of Cooley’s anemia (major beta thalassemia).

Final Diagnostic tests for Cooley's Anemia:

- 1. Hb Electrophoresis result indicate presence of HbF about 90%
- 2. DNA analysis searching for the β genes on the chromosome 11 (three are absence of two beta chains).

But when deletion of one beta chain **Minor β –Thalassemia** that characteristic by:

- 1-RBC is elevated over 5.5 million per mm^3 .
- 2-Not needs blood transfusion.
- 3-No hemolysis.



Laboratory diagnosis of Minor β -thalassemia:

1-CBC		2-Blood film:	3-Hb electrophoresis, the result may be as follow:	
Hb	8-10g/dl	1. microcytic, hypochromic 2. Target Cells, 3. Basophilic Stippling,	HbA	Over 60%
RBC c	>5.5 million /L		HbA2	4-7% It is the diagnostic test
MCV	50-70FL		HbF	Normal
RDW	Normal			
Retic-count	Mild raised			

Table 5 laboratory findings of minor trait beta thalassemia.

References:

- 1-Martin, A., & Thompson, A. A. (2013). Thalassemias. *Pediatric Clinics*, 60(6), 1383-1391.
- 2- Hoffbrand, A. V., & Steensma, D. P. (2019). Hoffbrand's essential haematology. John Wiley & Sons.
- 3-Shafique, F., Ali, S., Almansouri, T., Van Eeden, F., Shafi, N., Khalid, M., ... & Andleeb, S. (2021). Thalassemia, a human blood disorder. *Brazilian Journal of Biology*, 83.