

Thalassemia

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LEARNING OBJECTIVES

At the end of the lecture, you will be able to:

Define thalassemia

Know the types of thalassemia

Understand the diagnosis of thalassemia

Know the burden of thalassemia in the world & Jordan

Identify the pathogenesis & consequences of thalassemia

Recognize the strategies for control & prevention of thalassemia

Definition

Thalassemia is a genetic disorder that is due to mutations of the genes that are responsible for the production of hemoglobin in the blood.

*Thalassemia are a heterogeneous grouping of genetic disorders that result from a **decreased** synthesis of **alpha** or **beta** chains of hemoglobin (Hb)

Hemoglobin consists of **two proteins**, an **alpha**, & a **beta**

Etiology

It is caused by either a genetic **mutation** or a **deletion** of certain key gene fragments

Thalassemia is an **inherited disease**, meaning that at least **one of the parents** must **be a carrier** for the disease

As thalassemia is an inherited condition, **individuals with a family history of the condition are more likely to be affected**

Inheritance

If **both parents** possess **one gene mutation**, any children will have a **25% chance** of **inheriting a gene mutation**, regardless of whether the parents are symptomatic

If one or both parents possess **multiple gene mutations**, the **risk** of gene inheritance **increases**, and the child is more likely to experience symptoms

Burden of thalassemia

Thalassemia is highly prevalent in

Italian

Greek

Middle Eastern

Asian

African

Up to **20%** of world population **carries** the α -thalassemia genes

alpha-thalassemia is more common **in Southeast Asia**

Beta- thalassemia is more common among People with origins in the **Mediterranean**, as well as both **African** and **South Asian**

Thalassemia in Jordan

β -thalassemia is a common hereditary disorder, especially in the Middle East and is the most common hemoglobinopathy in Jordan with **The carrier prevalence rate of thalassemia in Jordan is currently reported as around 2–4%.**

† **in Jordan there were about 1500 thalassaemia patients with a prevalence rate of about 4 to 6% of Beta Thalassemia Major (BTM)** Jordan was among the nations that took special care in preventative measures in the **form of Premarital Screenings and Genetic Counselling (PMSGC).**

Thalassemia in Jordan

screenings helped **prevent the marriage of carriers** of the illness which were around **3.5%** of the population.

It was made clear that this measure had **decreased the incidence** of the disease **by 40 %** and that

medical professionals hoped the rate **to be halved**, similar to other Mediterranean countries.

Types of thalassemia

1- Alpha-thalassemia and

2- Beta-thalassemia

**Each of which has a different prevalence among certain ethnicities
or population groups.**

Alpha-Thalassemia

Alpha-thalassemia is caused by alpha-globin gene **deletion** which results in **reduced** or **absent** production of alpha-globin chains.

Alpha-thalassemia arises due to **insufficient synthesis** of **alpha hemoglobin** chains and an **excess of beta chains**

There are **four genes** on chromosome **16** that are required to produce the **alpha region** of hemoglobin, **two** of which are **inherited** from **each parent** of an individual.

Alpha-thalassemia is more common in Southeast Asia

Alpha-Thalassemia

The number of gene mutations corresponds to the severity of the condition as follows:

- 1- **One gene** : no signs or symptoms but may pass the disease on to children as a **silent carrier**
- 2- **Two gene**: mild signs and symptoms, referred to as alpha-thalassemia minor or **alpha-thalassemia trait**
- 3- **Three gene** : moderate to severe symptoms, referred to as alpha-thalassemia intermedia or **hemoglobin H disease**
- 4- **Four gene** mutations: often **fatal** before or shortly after childbirth, referred to as alpha-thalassemia major or **hydrops fetalis**

Beta-Thalassemia

- Beta-thalassemia occurs **due to insufficient synthesis** of **beta hemoglobin chains** and an excess of alpha chains.
- **There are two genes** on **chromosome 11** that are required to produce the beta region of the hemoglobin chain
- each of which is inherited from **one parent**

Beta-Thalassemia

The number of gene mutations corresponds to the severity of the condition **as follows:**

1-One gene mutation: **mild signs or symptoms**, referred to as beta-thalassemia **minor** or thalassemia trait

2-Two gene mutations: moderate to severe symptoms, referred to as beta-thalassemia major or **Cooley's anemia.**

Beta-thalassemia major (Cooley's anemia)

babies born with two mutated beta hemoglobin genes are usually healthy at birth, but disease starts to manifest after 6 months of life when fetal hemoglobin(Hb-gamma) disappears and is replaced by adult Hb.

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➔ People with origins in the Mediterranean, as well as both
➔ African and South Asian areas, are more likely to be affected by beta-thalassemia

Beta-thalassemia major

The WHO estimates that Beta-thalassemia affects **2.9%** of the world's population

	Prevalence
Eastern Mediterranean	: 2-18%
Europe:	0-19%
Western Pacific	0-13%
Sub-Saharan Africa	0-12%
Southeast Asia	0-11%
Americas:	0-3%

Thalassemia presentation

Thalassemia presentation **varies** widely depending on the **type and severity**.

- **Skin; Pallor** due to anemia and jaundice due to hyperbilirubinemia resulting from intravascular hemolysis.
fatigue due to anemia as the first presenting symptom.
- **Extremities examination: ulcerations. bronze skin as a result of** chronic iron deposition due to multiple transfusions
- **Musculoskeletal:** Extra medullary expansion results in **deformed facial and other skeletal bones** and an appearance known as **chipmunk face** وجه السنجاب
- **Cardiac;** Iron deposition can **disrupt the cardiac rhythm**, and the result is various **arrhythmias**.
Due to chronic anemia, overt **heart failure** can also **result**.

Thalassemia presentation

Abdominal: Chronic hyperbilirubinemia can lead to precipitation of bilirubin **gall stones** and manifest as typical colicky pain of **cholelithiasis**.

Hepatosplenomegaly can result from chronic iron deposition

Hepatic involvement is a common finding in thalassemia, particularly due to chronic iron deposition. **Chronic liver failure** or **cirrhosis** or transfusion-related **viral hepatitis**.

Slow Growth Rates: Particular attention should focus on the child's growth and development according to age.

Anemia can **inhibit a** child's growth rate, and thalassemia can cause a **delay in puberty**.

Thalassemia presentation

Endocrinopathies; Deposition of iron in the

- ✦ Pancreas can lead to **diabetes mellitus**;
- ✦ Thyroid or Parathyroid glands can lead to **hypothyroidism** and **hypoparathyroidism**, respectively.
- ✦ **Joints** leads to chronic **arthropathies**.
- ✦ **Brain**, iron prefers to accumulate in the substantia nigra and manifests as early-onset **Parkinson's disease** and various other psychiatry problems. (disabilities related to the brain, nerves, bones and muscles)

Diagnosis of thalassemia

Several laboratory tests have been developed to screen and diagnose thalassemia

a) Complete blood count (CBC): CBC is often the first investigation in a suspected case of thalassemia

CBC showing **low Hb** and **low MCV** is the first indication of **thalassemia**, after ruling out iron deficiency as the cause of anemia.

b) The calculation of the Mentzer index (mean corpuscular volume divided by red cell count) is useful.

Mentzer index:

- **lower than 13** suggests that the patient has **thalassemia**,
- **more than 13** suggests that the patient has anemia due to **iron deficiency**

Diagnosis of thalassemia

c) Peripheral blood smear: is next, to assess additional red cell properties. Thalassemia can present with the following findings on the peripheral blood smear :**Microcytic cells**

d) Iron studies (*serum iron, ferritin, unsaturated iron-binding capacity (UIBC), total iron-binding capacity*)

e) Erythrocyte porphyrin levels may be checked to distinguish an unclear **beta-thalassemia minor** diagnosis from **iron deficiency or lead poisoning**

Diagnosis of thalassemia

f) Hemoglobin electrophoresis:

Hemoglobinopathy (Hb) evaluation assesses the type and relative amounts of hemoglobin present in red blood cells.

i-Hemoglobin A (HbA); Composed of both alpha and beta-globin chains, is the type of Hb that typically makes up **95% to 98% of hemoglobin for adults.**

ii-Hemoglobin A2 (HbA2) is normally **2% to 3%** of Hb while **iii-hemoglobin F** usually makes up **less than 2%** of Hb in adults

Diagnosis of thalassemia

Beta thalassemia: disturbs the balance of beta and alpha hemoglobin chain formation.

→ Patients with the **beta-thalassemia major** usually have

‡ **larger percentages of HbF and HbA2 and**

‡ **Absent or very low HbA.**

Those with **beta-thalassemia minor** usually have a **mild elevation of HbA2 and mild decrease of HbA.**

→ **HbH** is a less common form of hemoglobin that may be seen in some cases of **alpha thalassemia.**

→ Hemoglobinopathy (Hb) assessment is **used for prenatal screening when parents** are at **high risk for hemoglobin abnormalities**

Management

Mild thalassemia (Hb: 6 to 10g/dl):

Signs and symptoms are generally mild with thalassemia minor and **little if any, treatment** is needed.

Occasionally, patients may need a **blood transfusion**, particularly **after surgery, following childbirth**, or to help manage thalassemia complications

Moderate to severe thalassemia

Moderate to severe thalassemia (Hb less than 5 to 6g/dl):

Frequent blood transfusions: More severe forms of thalassemia often require **regular blood transfusions**, possibly every few weeks.

The goal is to maintain Hb at around **9-10 mg/dl**.

To limit transfusion-related complications, **washed, packed red blood cells (RBCs)** at approximately **8 to 15 mL** cells per kilogram (kg) of body weight **over 1 to 2 hours** are recommended

Management

Chelation therapy: Due to chronic transfusions, iron starts to get deposited in various organs of the body.

✚ **Iron** chelators (deferasirox, deferoxamine, deferiprone) are given concomitantly to remove extra iron from the body.

➔ **Stem cell transplant:** Stem cell transplant, (bone marrow transplant), is a potential option in selected cases, such as **children born with severe thalassemia.**

Gene therapy: It is the latest advancement in severe thalassemia management.

Prevention

In most cases, we **can't prevent thalassemia**.
If there is a case of thalassemia, or **carrier of thalassemia gene**, **genetic counselor is recommended for guidance for having children in a future**

Prenatal diagnosis and genetic counselling
Gene Carriers

It is important for individuals who are known to carry gene mutations that may lead to thalassemia to **seek medical advice before** deciding to have children

The End



Thank You

